

## Ticagrelor vs Aspirin in Patients undergoing Coronary-Artery Bypass Grafting

*Heribert Schunkert, MD*

on behalf of  
the TiCAB Investigators



# TiCAB – an investigator initiated trial

## Sponsor

Deutsches Herzzentrum München  
Lazarettstr. 36  
80636 Munich, Germany



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A Randomized, Parallel Group, Double-Blind Study of Ticagrelor Compared with Aspirin for  
Prevention of Vascular Events in Patients Undergoing  
Coronary Artery Bypass Graft Operation\*  
April 2013 to May 2018

\* de Waha et al Am Heart J. 2016;179:69-76





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## Unmet Needs After CABG Surgery

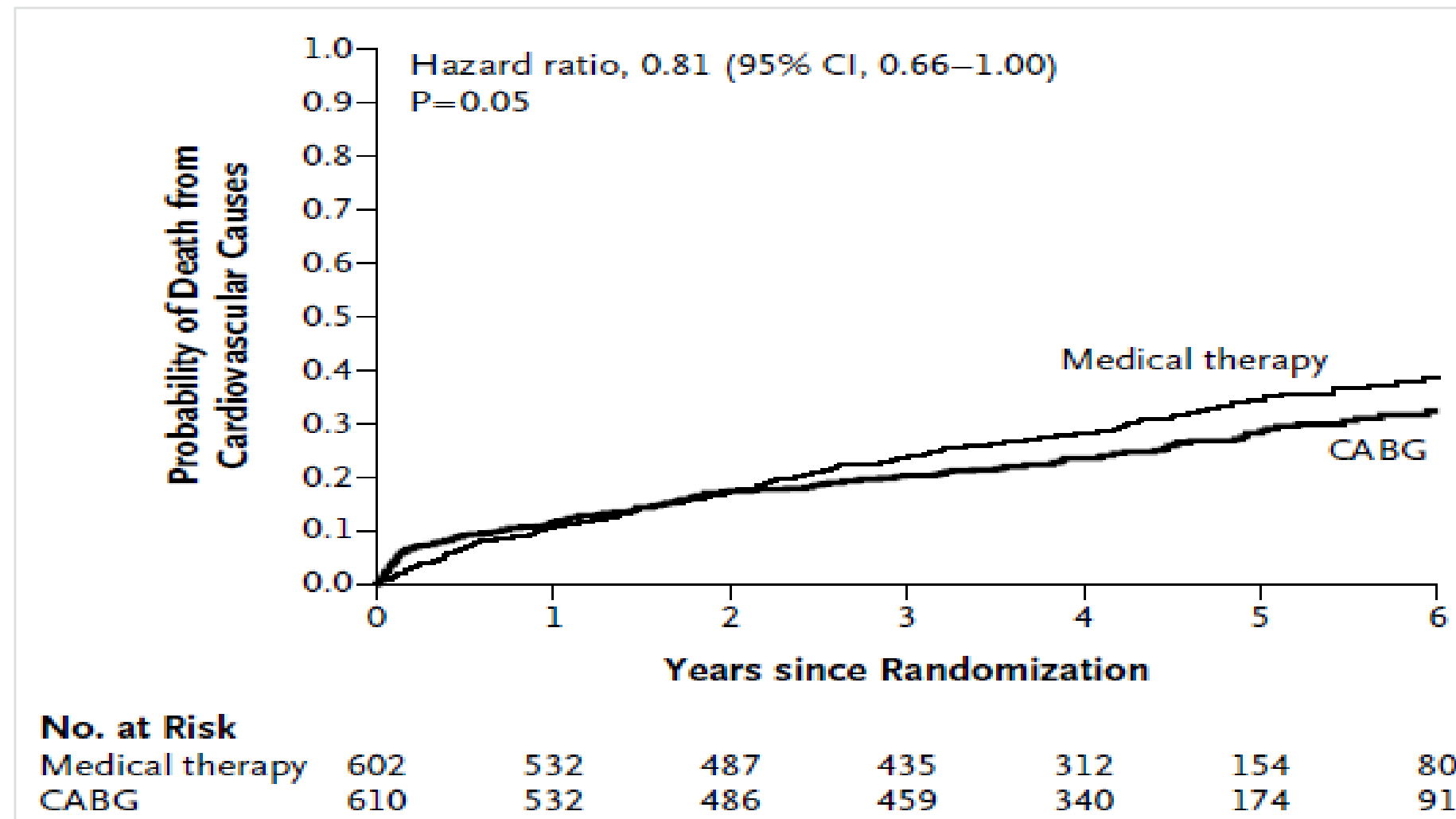
- Graft failure is related to major adverse events
- Graft failure peaks in first year post surgery
- More intense platelet inhibition has been shown to prevent graft failure



## Study Hypothesis

Ticagrelor, as compared to aspirin,  
reduces major adverse cardiovascular events  
within one year after CABG operation.

# TiCAB: Power calculation



**STICH** trial (CHF):

Mortality 12% at 1 year

N Engl J Med 2009

**SYNTAX** trial (3VD and LM):

MACCE rate 12.4% at 1 year

N Engl J Med 2009

**PLATO-CABG** (ACS): MACCE

Ticagrelor/ Aspirin 10.6%

Clopidogrel/ Aspirin: 13.1%

JACC 2011

**TiCAB** (3VG, LM, 2VD+EF<50% - stable CAD and ACS)

Primary end point: CV death, MI, stroke and revascularisation

- estimated event rate: 13% in the control group
- Two-sided  $\alpha$  level of 0.0492 (0.05 adjusted for a planned interim analysis)
- Power of 0.80
- Expected relative risk of 0.775 in the active group
- Total of 3760 patients required

## Secondary Endpoints @ 12 months

- Safety endpoint: Incidence of major bleeding events
- Components of the primary endpoint:
  - Cardiovascular death
  - Myocardial infarction
  - Stroke
  - Recurrent revascularization



## Study Design

- Randomized
- Double blind
- Parallel group
- International multicenter
- Phase III study



## Inclusion Criteria

1. Patients 18 years of age or older – and
2. Informed, written consent by the patient – and
3. Indication for CABG surgery – and
  - coronary three vessel disease, or
  - left main stenosis, or
  - two vessel disease with impaired EF (< 50%)

## Exclusion Criteria

1. Cardiogenic shock, haemodynamic instability
2. Indication for oral anticoagulation or dual antiplatelet therapy
3. Need for concomitant non-coronary surgery (e.g. valve replacement)
4. Contraindication for Aspirin or Ticagrelor use (e.g. known allergy)
- 5....



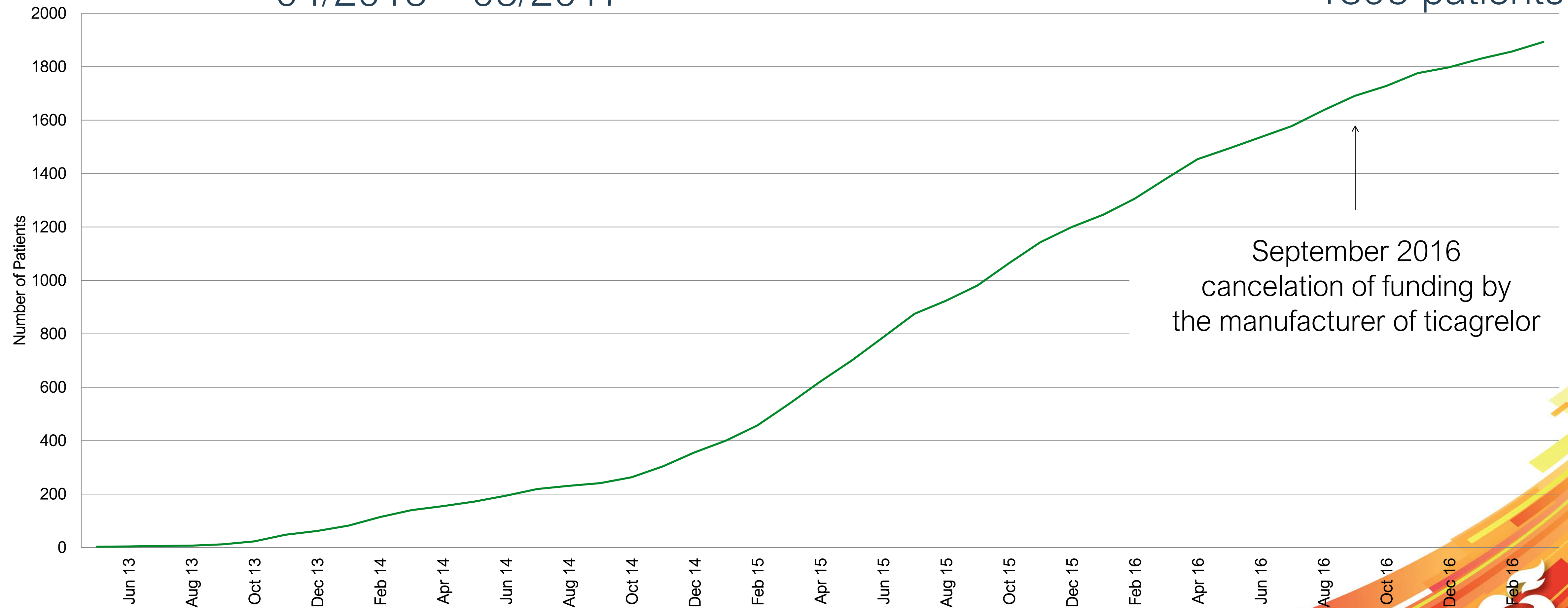
## Follow-up

- 1<sup>st</sup> Visit: CABG - Hospital visit
- 2<sup>nd</sup> Visit: 3 months after CABG - Hospital visit
- 3<sup>rd</sup> Visit: 6 months after CABG - Telephone visit
- 4<sup>th</sup> Visit: 9 months after CABG - Telephone visit
- 5<sup>th</sup> Visit: 12 months after CABG - Hospital visit

# TiCAB Trial - Recruitment

Recruitment (cumulative)  
04/2013 – 03/2017

Total recruitment:  
1893 patients

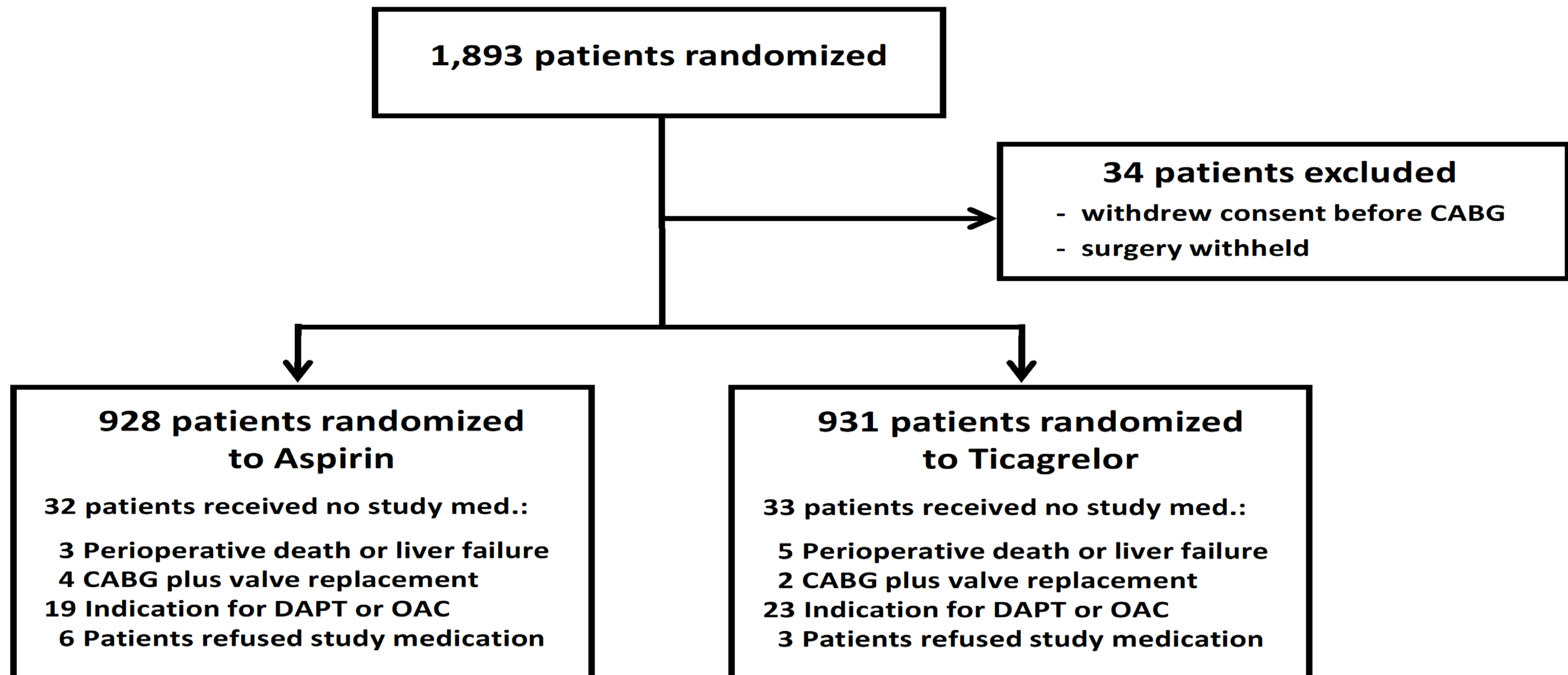




## Follow-up

- The trial was continued with in-house funding of the German Heart Center
- The planned interim analysis by the DSMB was scheduled for March 2018
- The DSMB suggested the trial to be stopped

## Trial Enrollment, Randomization and Follow-up





## Baseline Characteristics (I)

Characteristics	Aspirin Group (n=928)	Ticagrelor Gr. (n=931)
Male sex, no. (%)	785 (84.6)	794 (85.3)
Age – years	67.0 ± 10.2	66.4 ± 10.1
Stable angina, no. (%)	646 (69.6)	642 (69.0)
Unstable angina, no. (%)	117 (12.6)	126 (13.5)
Non-ST-elevation myocardial infarction, no. (%)	165 (17.8)	163 (17.5)
History of myocardial infarction, no. (%)	204 (22.0)	218 (23.4)
<b>Cardiovascular risk factors</b>		
Hypertension, no. (%)	836 (90.1)	836 (89.8)
Hyperlipidemia, no. (%)	754 (81.3)	765 (82.2)
Smoking, no. (%)	187 (20.2)	200 (21.5)
Ex-Smoking, no. (%)	321 (34.6)	320 (34.4)
Diabetes, no. (%)	330 (35.6)	338 (36.3)
<b>Left ventricular ejection fraction</b>		
< 30 %, no. (%)	16 (1.8)	17 (1.9)
30%-50%, no. (%)	232 (25.6)	225 (24.7)
>50%, no. (%)	646 (71.1)	659 (72.4)



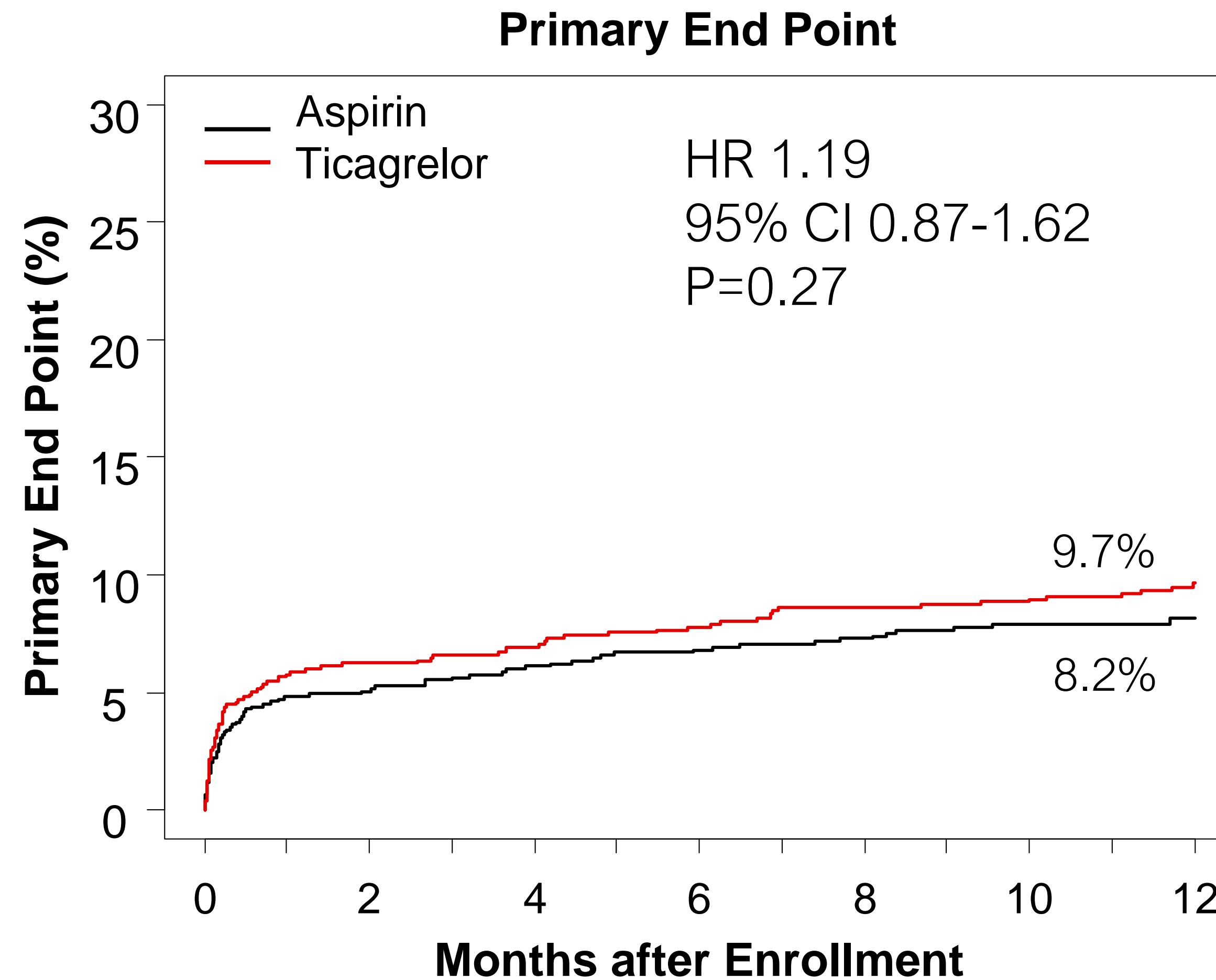
## Baseline Characteristics (II)

Characteristics	Aspirin Group (n=928)	Ticagrelor Gr. (n=931)
<b>Extent of coronary artery disease</b>		
Three vessel disease, no. (%)	858 (92.5)	855 (91.8)
Two vessel disease and EF (< 50 %), no. (%)	60 (6.5)	67 (7.2)
Left main disease, no. (%)	365 (39.3)	387 (41.6)
<b>Medication use</b>		
Aspirin, no. (%)	731 (78.8)	727 (78.1)
P2Y12-Inhibitor, no. (%)	81 (8.7)	98 (10.5)
Ticagrelor, no. (%)	26 (2.8)	37 (4.0)
Prasugrel, no. (%)	0 (0.0)	4 (0.4)
Clopidogrel, no. (%)	55 (5.9)	57 (6.1)
Oral anticoagulant, no. (%)	4 (0.4)	1 (0.1)
β-blockers, no. (%)	606 (65.3)	635 (68.2)
ACEI or ARB, no. (%)	198 (21.3)	242 (26.0)
Calcium antagonist, no. (%)	202 (21.8)	199 (21.4)
Diuretics, no. (%)	288 (31.0)	286 (30.7)
Statins, no. (%)	779 (83.9)	776 (83.4)
Nitrates, no. (%)	53 (5.7)	50 (5.4)
Proton pump inhibitor, no. (%)	264 (28.4)	304 (32.7)



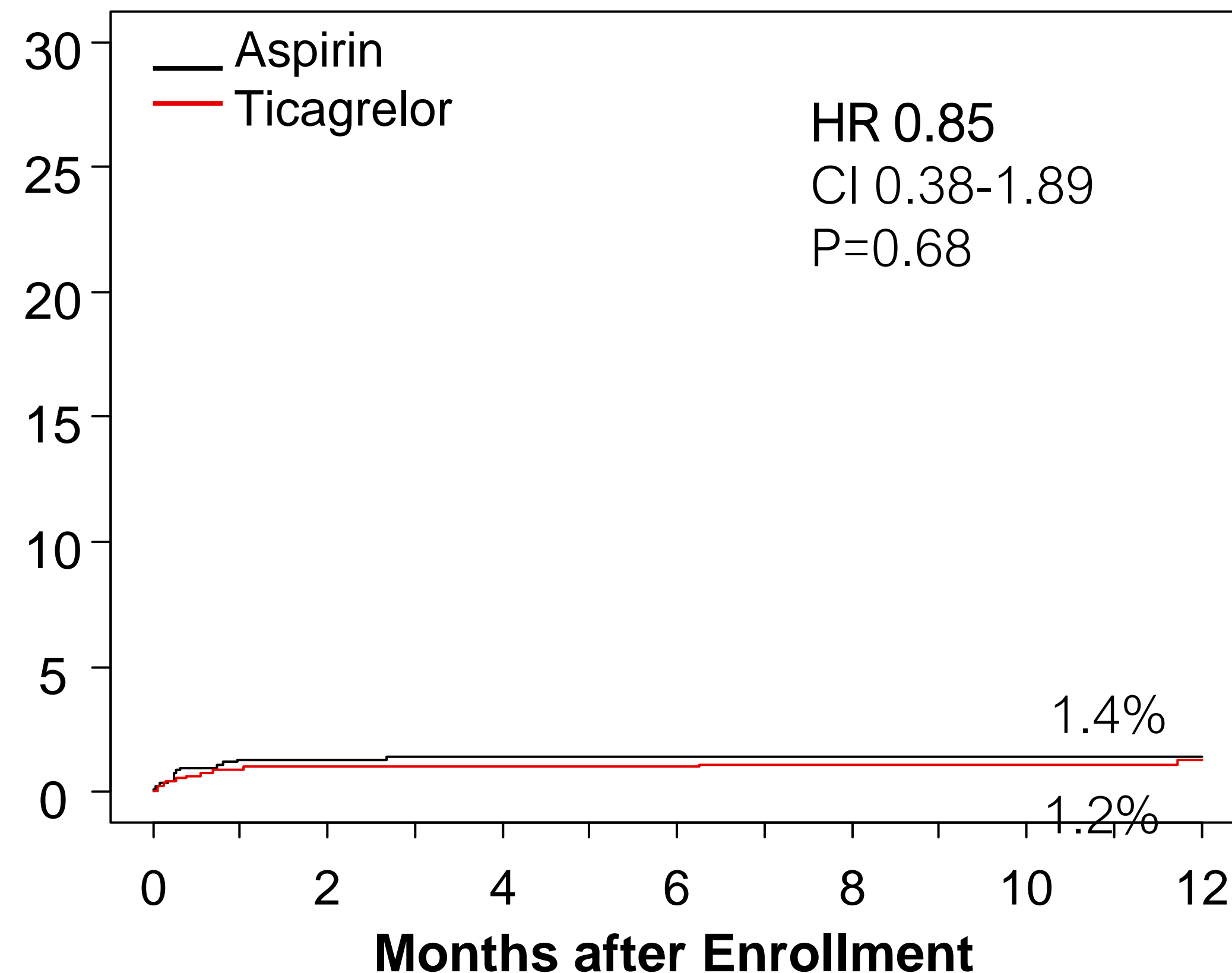


## Results – CV death, MI, stroke, repeat revascularization

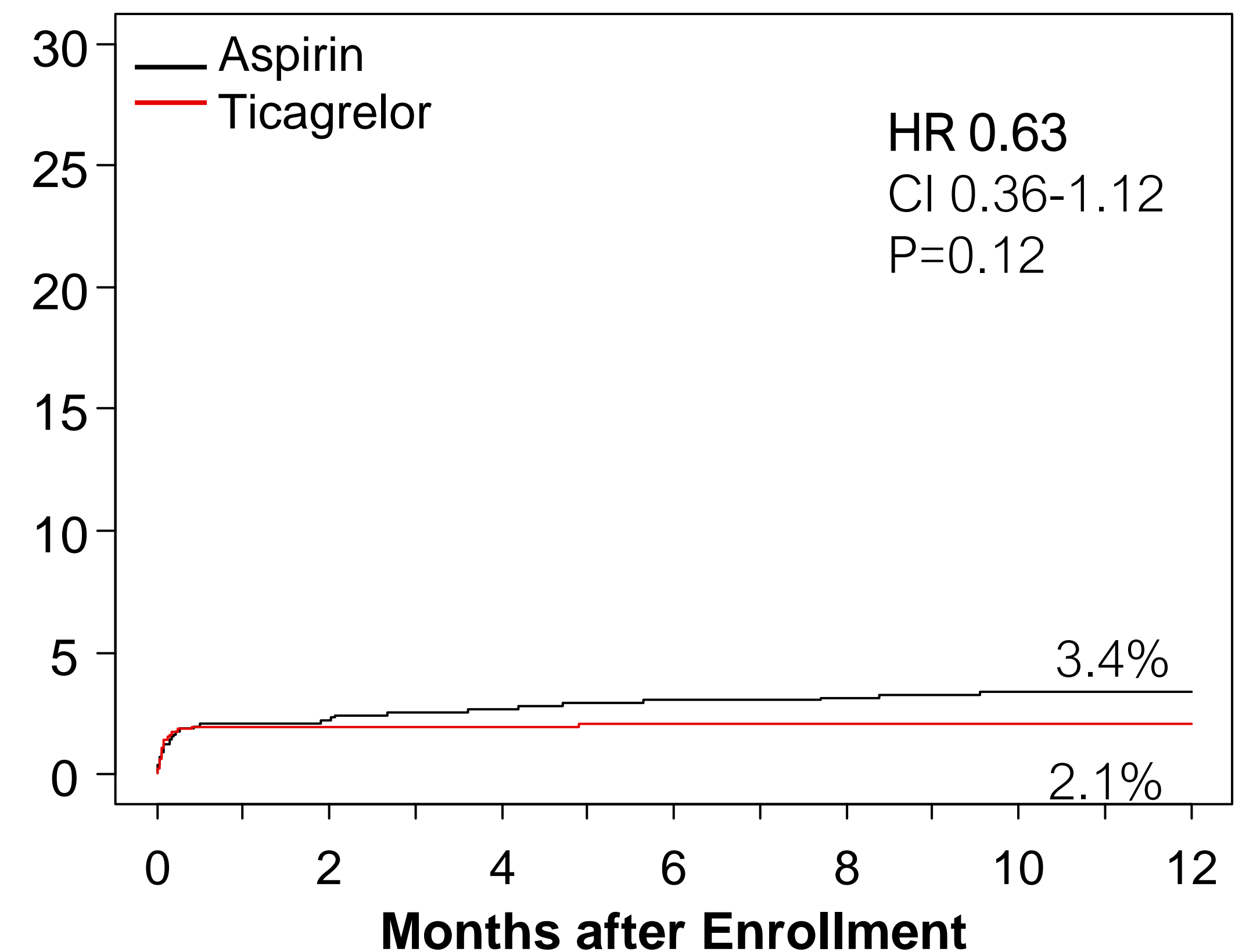


## Results – Secondary Endpoints

### Cardiovascular Death



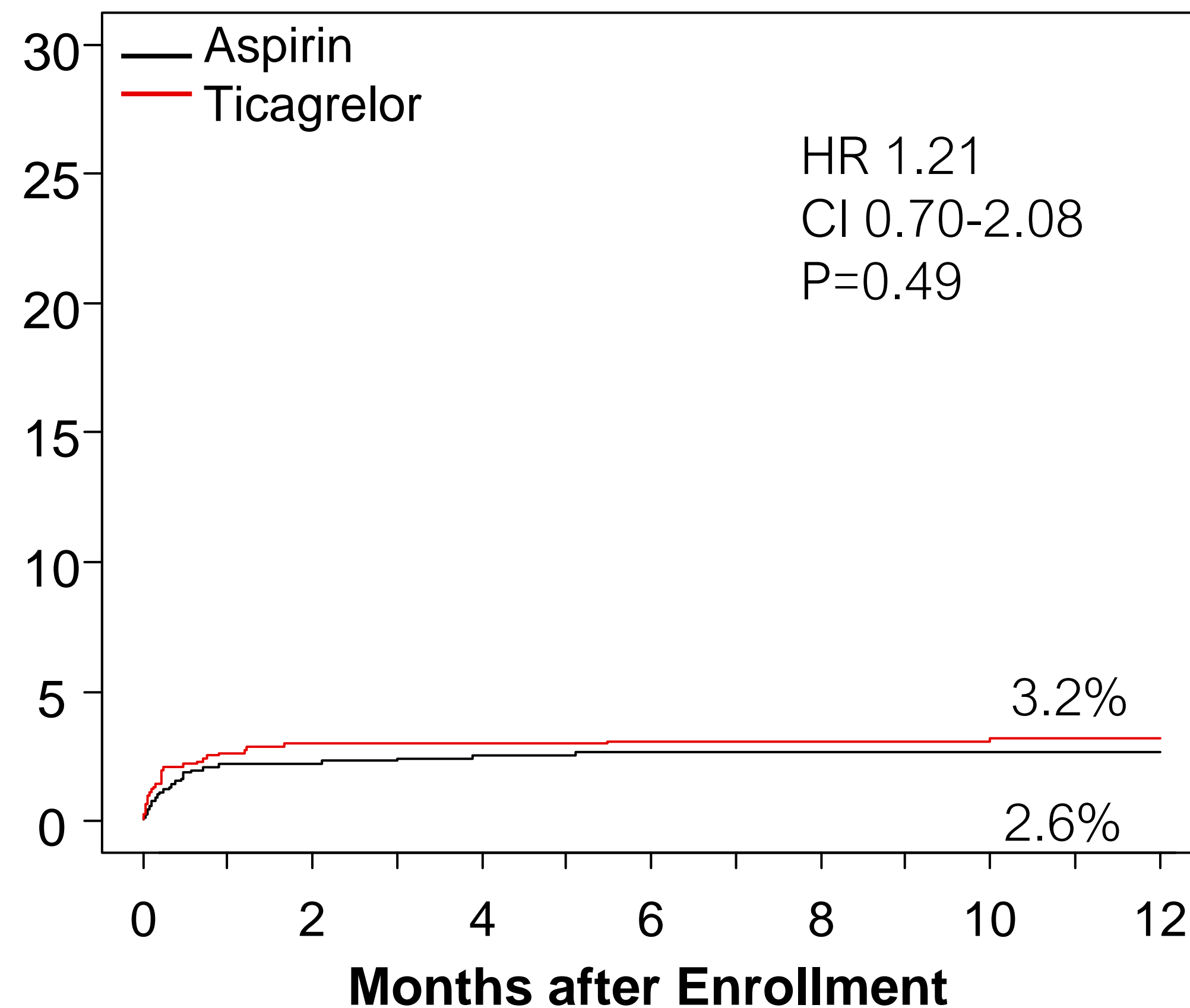
### Myocardial infarction



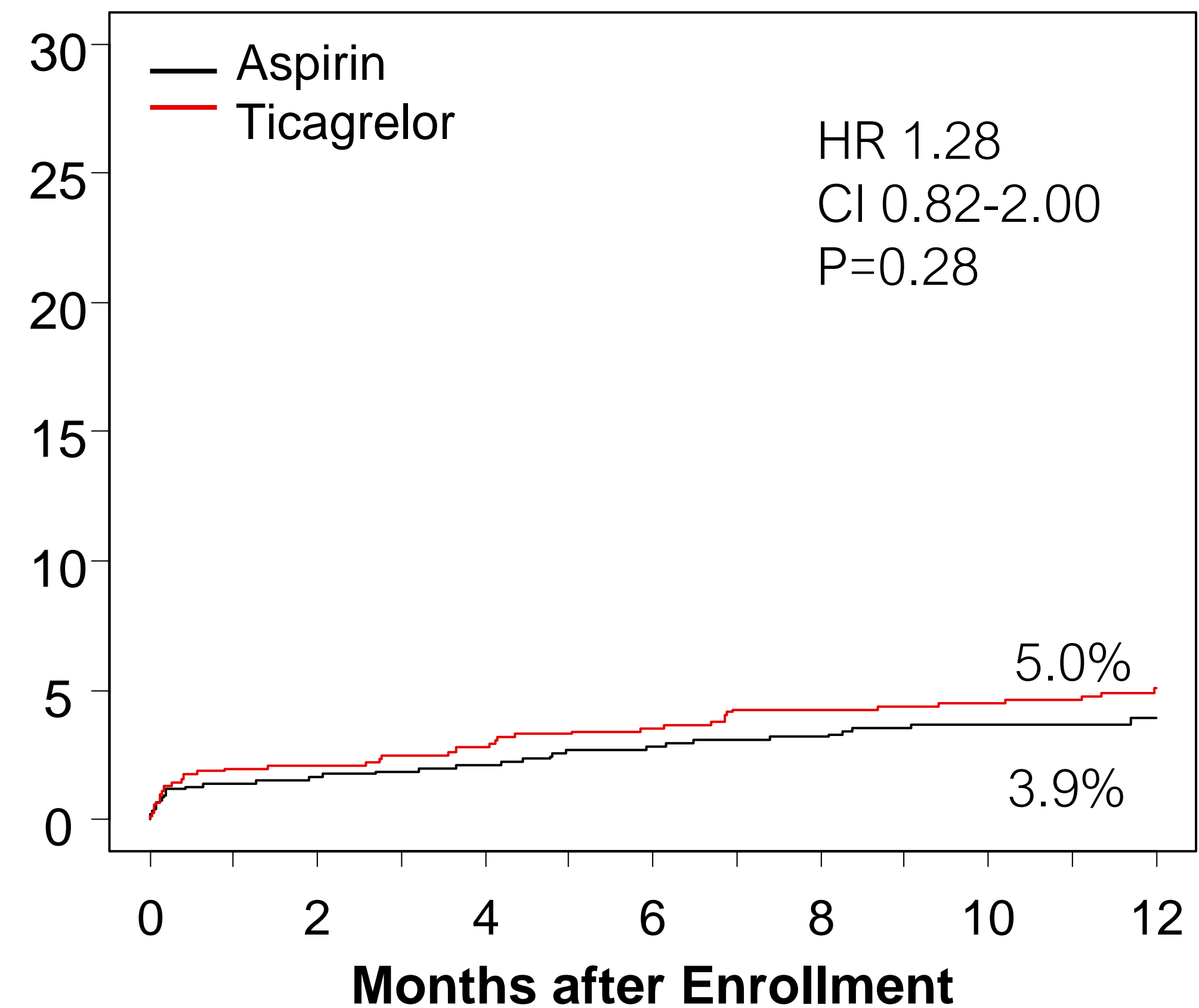


## Results – Secondary Endpoints

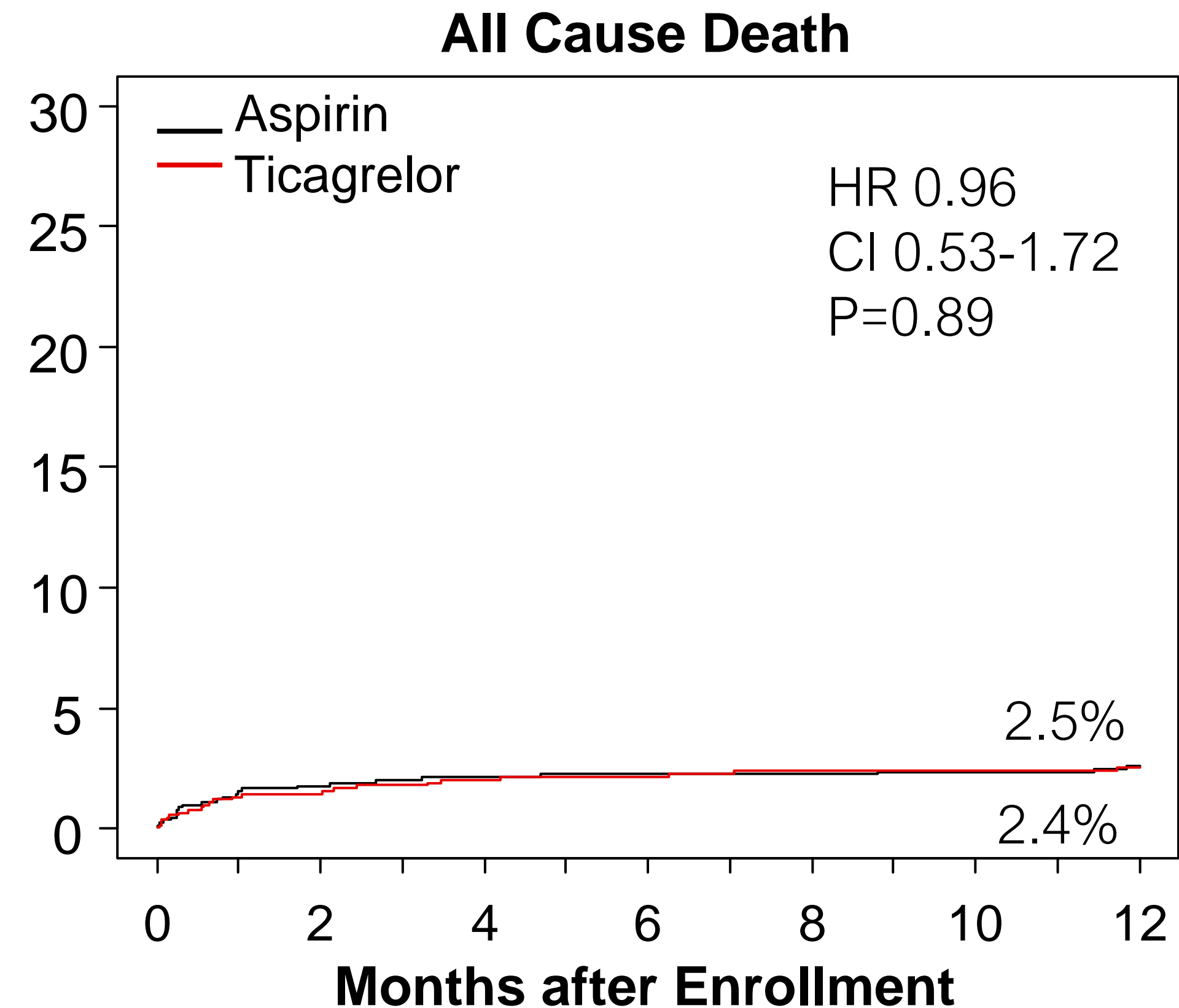
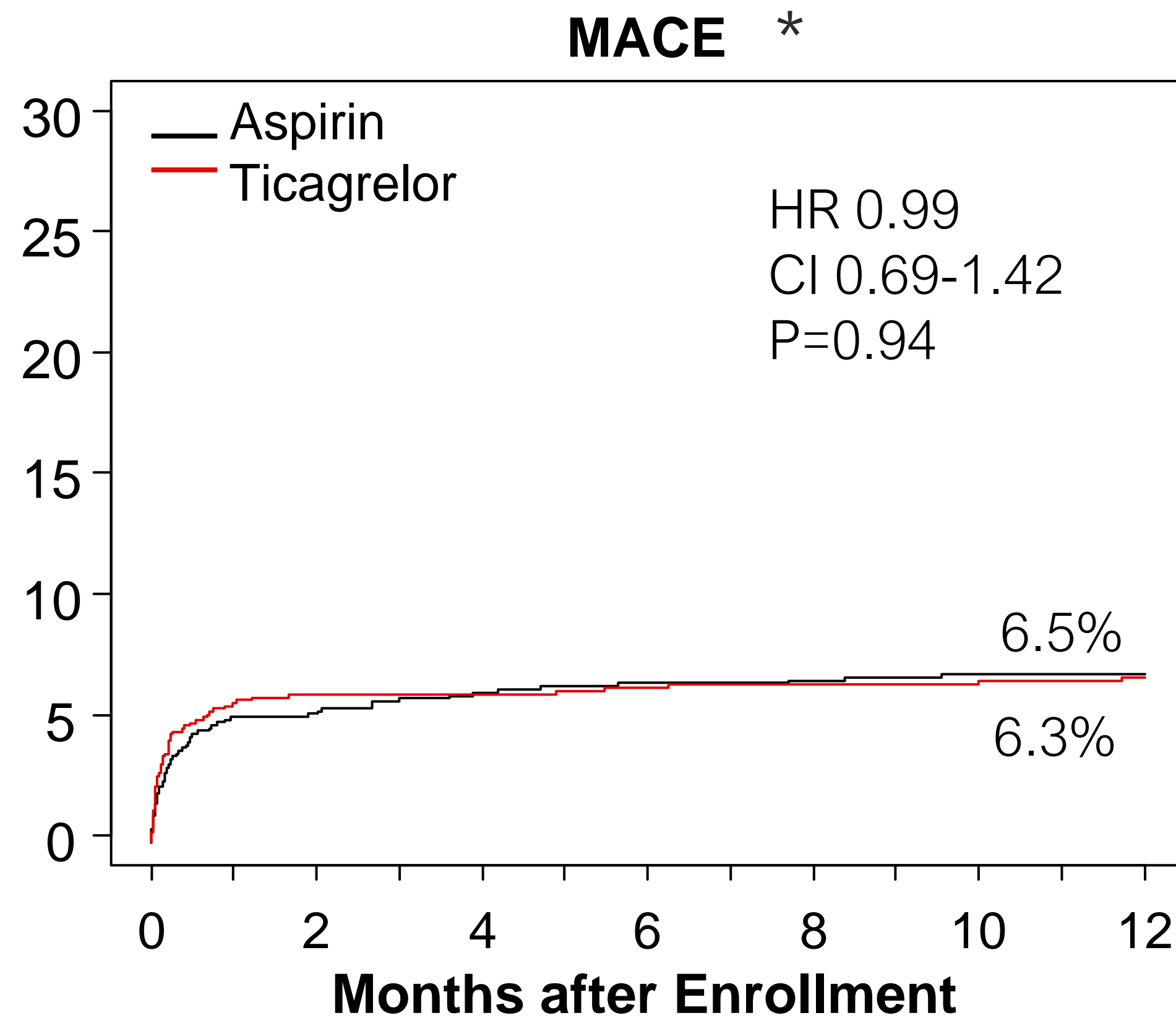
Stroke



Revascularization



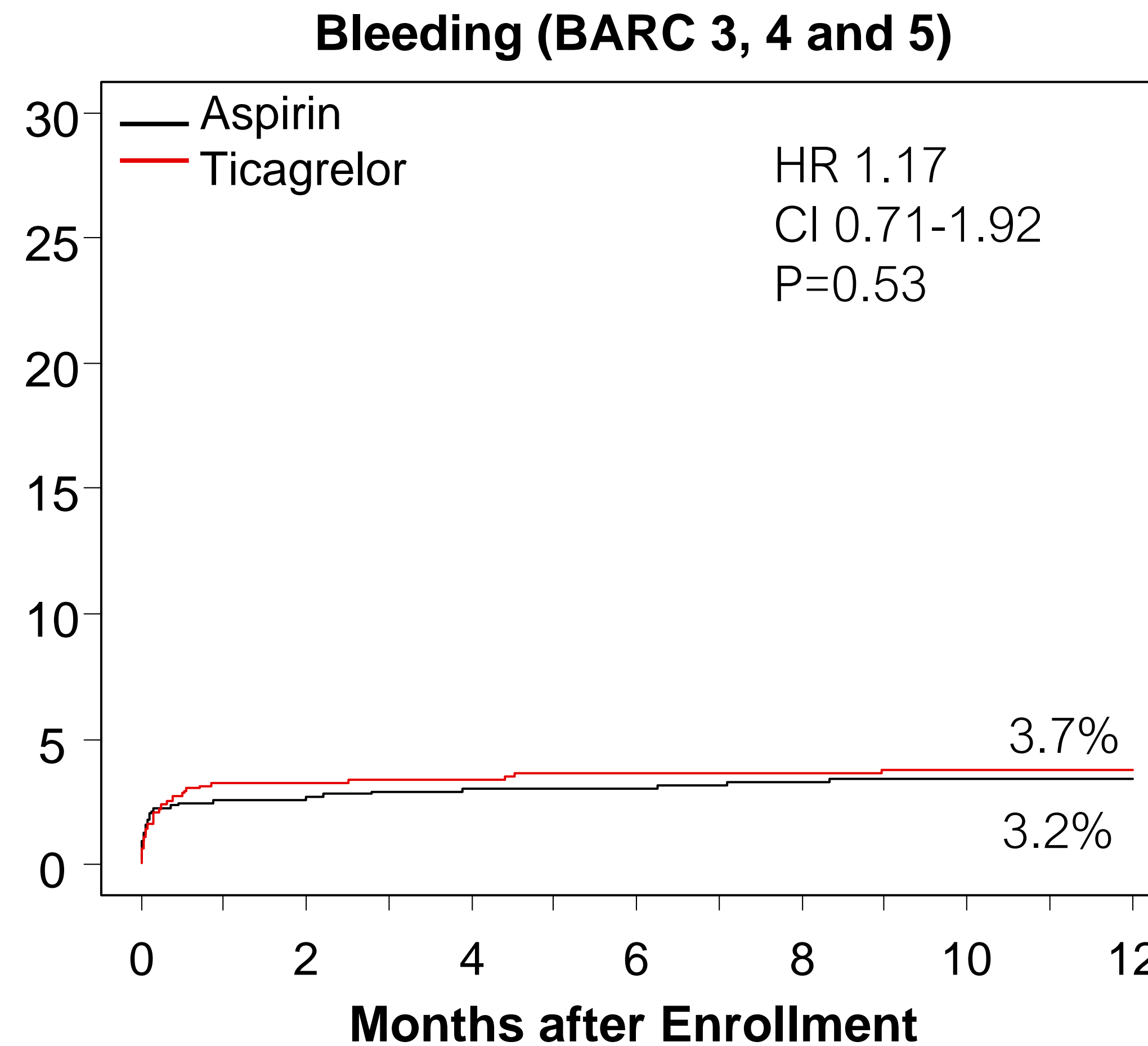
## Results – MACE and Total mortality



\*CV death, myocardial infarction or stroke

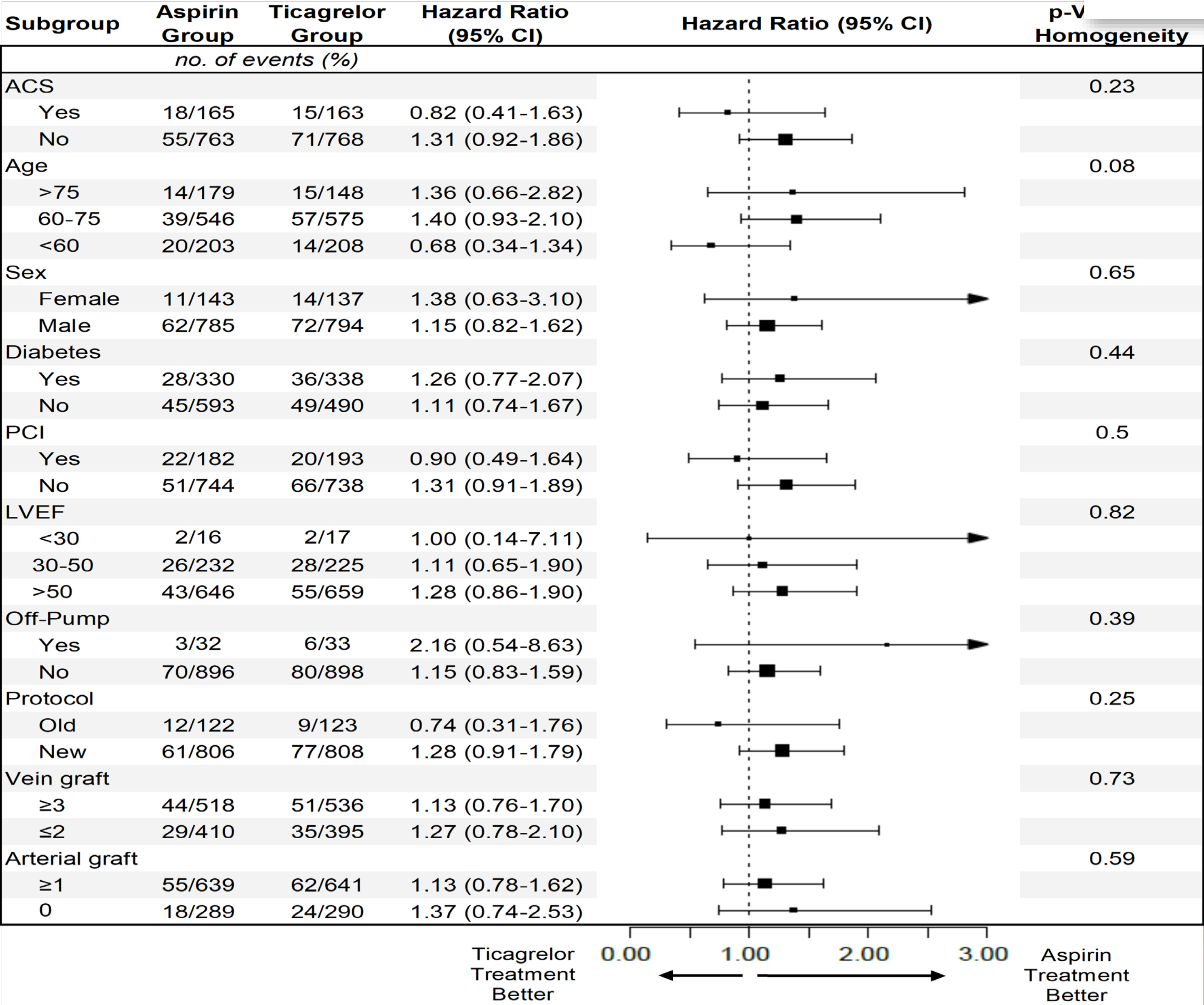


## Results – Bleeding events



# Aspirin vs Ticagrelor after CABG - TiCAB Trial

## Results – Primary Endpoint Subgroup analysis





## Limitations of the Study

- The event rates were lower than expected
- The study was terminated early after half of the anticipated patients were included
- A main source of funding terminated the contract
- Ticagrelor displayed no signal for better outcome
- The DSMB suggested to stop recruitment

## Conclusion of the Study

The use of ticagrelor monotherapy instead of aspirin monotherapy in patients undergoing CABG did not significantly impact the rates of major CV events nor major bleeding events.

# Aspirin vs Ticagrelor after CABG - TiCAB Trial

Thank you for your attention!





# *THANK YOU!*



**SCIENTIFIC** 20  
**SESSIONS** 18



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des Freistaates Bayern  
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