Prasugrel versus clopidogrel for patients with unstable angina/non-ST-segment elevation myocardial infarction who are medically managed after angiographic triage — Results from the TRILOGY ACS Trial

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On behalf of the TRILOGY ACS Investigators

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Authors and Disclosures*

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**For all other authors, see MT Roe et al, NEJM 2012*

Angiography Background

- The proportion of ACS (UA/NSTEMI) patients worldwide who are managed medically without revascularization (PCI or CABG) is 40–60%. This includes 2 distinct sets of patients:
  - triaged to medical therapy after angiography
  - for whom angiography is not performed
- Prasugrel, a thienopyridine $P2Y_{12}$ inhibitor, improved ischemic outcomes in ACS patients undergoing PCI in the TRITON-TIMI 38 trial, with an increase in major bleeding.

Wiviott SD et al NEJM 2007

Primary Efficacy Endpoint and TIMI Major Bleeding Through 30 Months

(Age < 75 years, N = 7243)

Prasugrel
Clopidogrel

Endpoint (%)

20
15
10
5
0

0
180
360
540
720
900

Days

HR (95% CI):
0.91 (0.79, 1.05)
P = 0.21

16.0% *Primary Efficacy Endpoint*
13.9%

HR (95% CI):
1.31 (0.81, 2.11)
P = 0.27

2.1% *TIMI Major Bleeding*
1.5%

Roe MT NEJM 2012

Prespecified Analysis of Angiographic Cohort

ITT Population
N = 9326

Primary Population
Age < 75
N = 7243

Age ≥ 75
N = 2083

Triaged after Angiography*
N = 3085 (43%)

Trigaged without Angiography*
N = 4158 (57%)

Randomized to Prasugrel
N = 1524

Randomized to Clopidogrel
N = 1561

Randomized to Prasugrel
N = 2096

Randomized to Clopidogrel
N = 2062

*For angiography vs no angiography comparisons — p-values unadjusted, for prasugrel vs clopidogrel - p-value adjusted for clopidogrel stratum

Incidence of Outcomes by Angiography Status

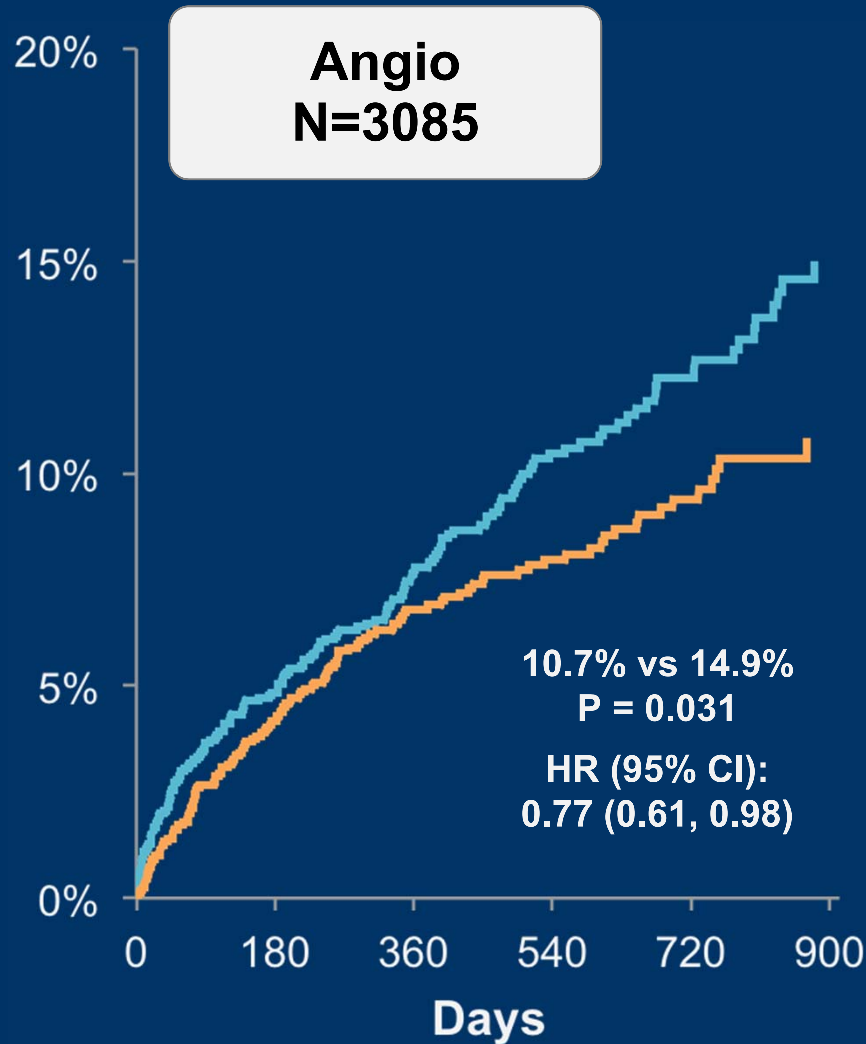
(Age < 75 years)

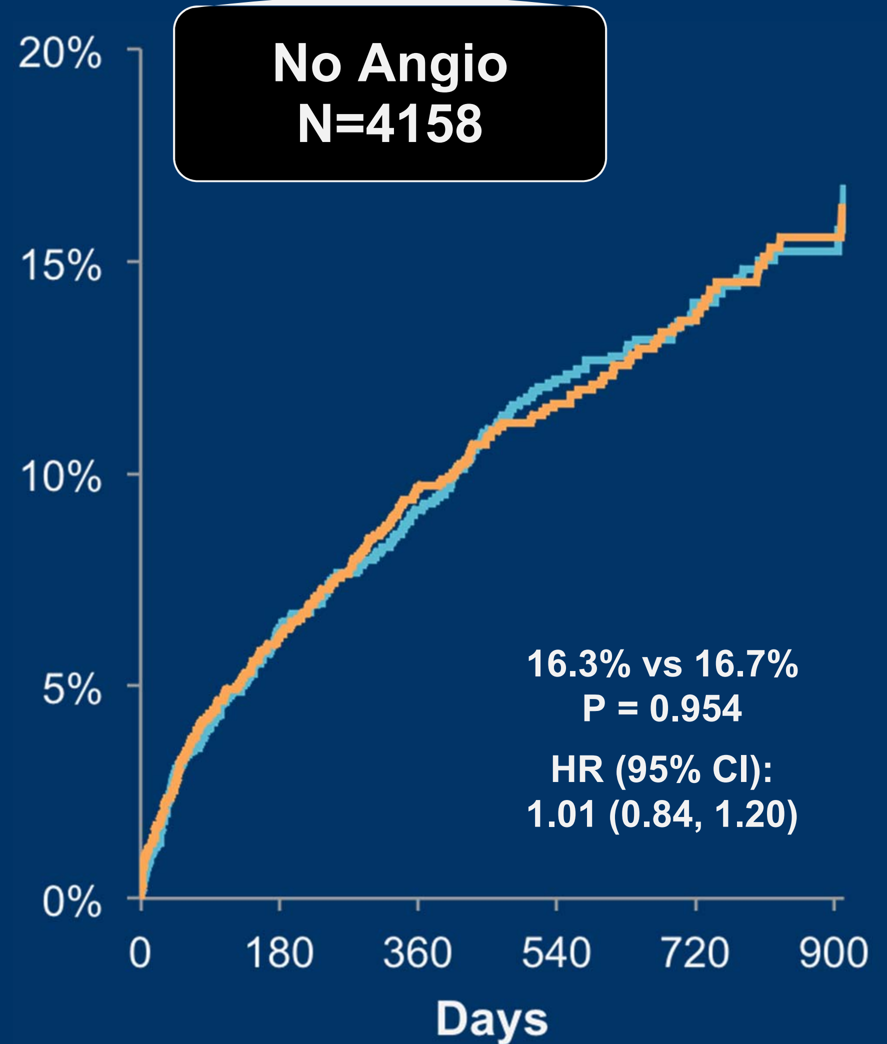
	Angio	No Angio	P
CVD/MI/Stroke	12.8%	16.5%	P < 0.001
CVD	4.7%	8.2%	P < 0.001
MI	8.7%	9.9%	P = 0.11
Stroke	1.5%	2.1%	P = 0.47
Death	5.8%	9.6%	P < 0.001
TIMI Major	2.0%	1.6%	P = 0.09
TIMI Major/Minor	3.2%	2.3%	P = 0.04

Y-axis: 0%, 5%, 10%, 15%, 20%

Primary Efficacy Endpoint to 30 Months

(Age < 75 years)

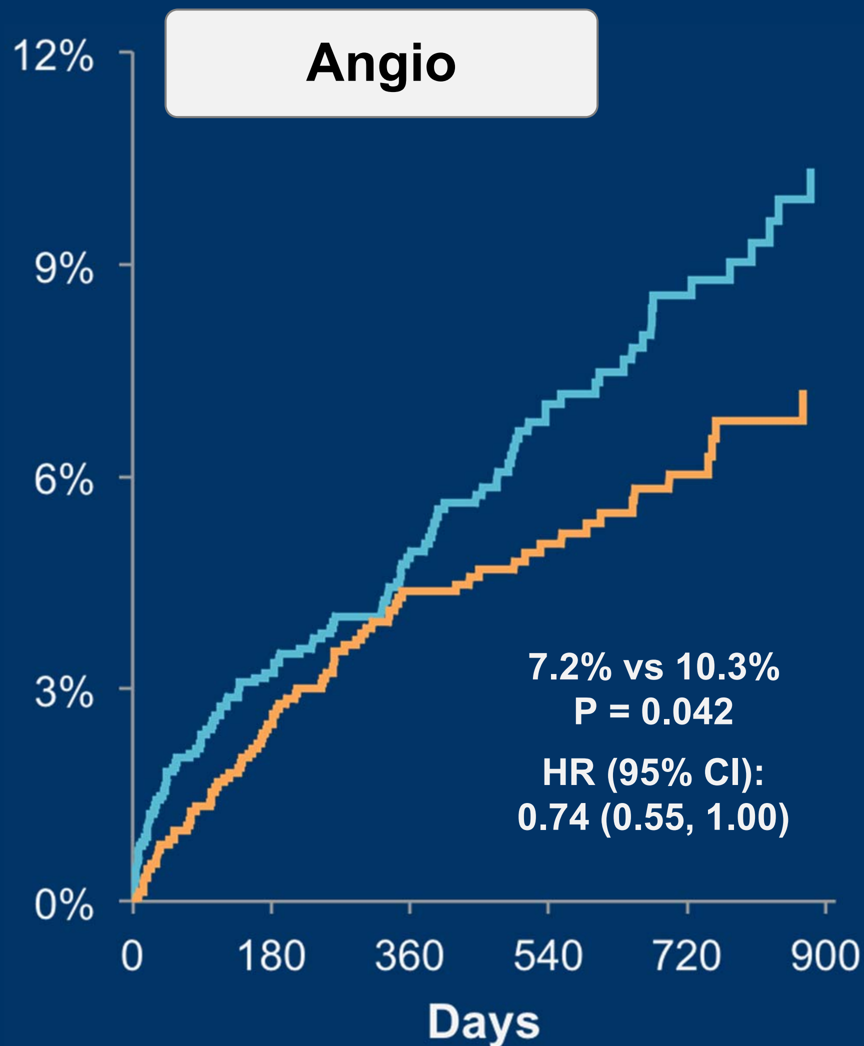


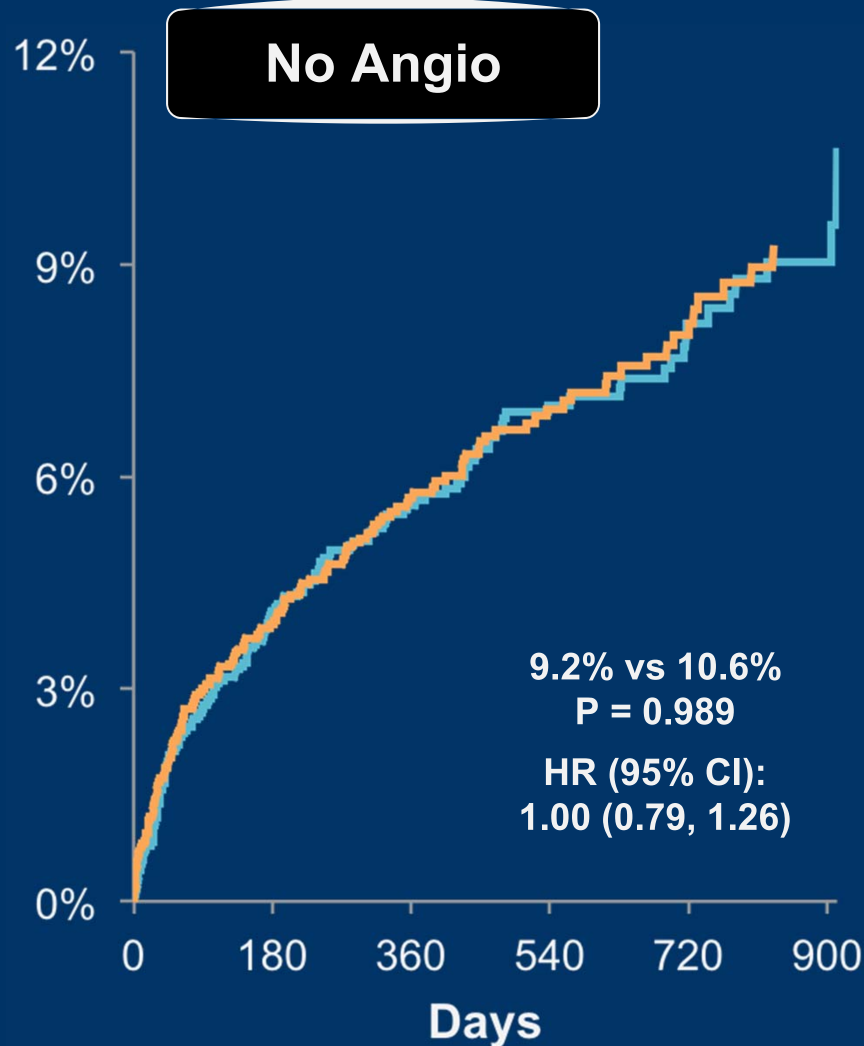


P interaction = 0.08

Myocardial Infarction

Prasugrel — Clopidogrel



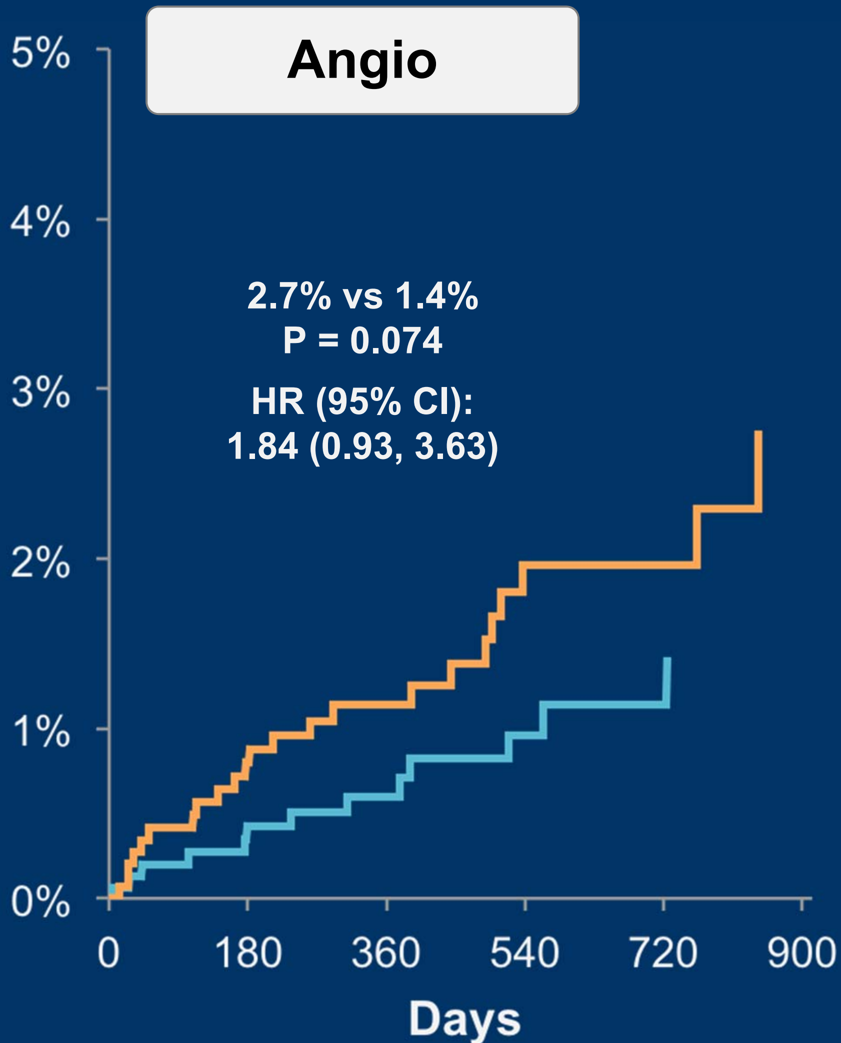


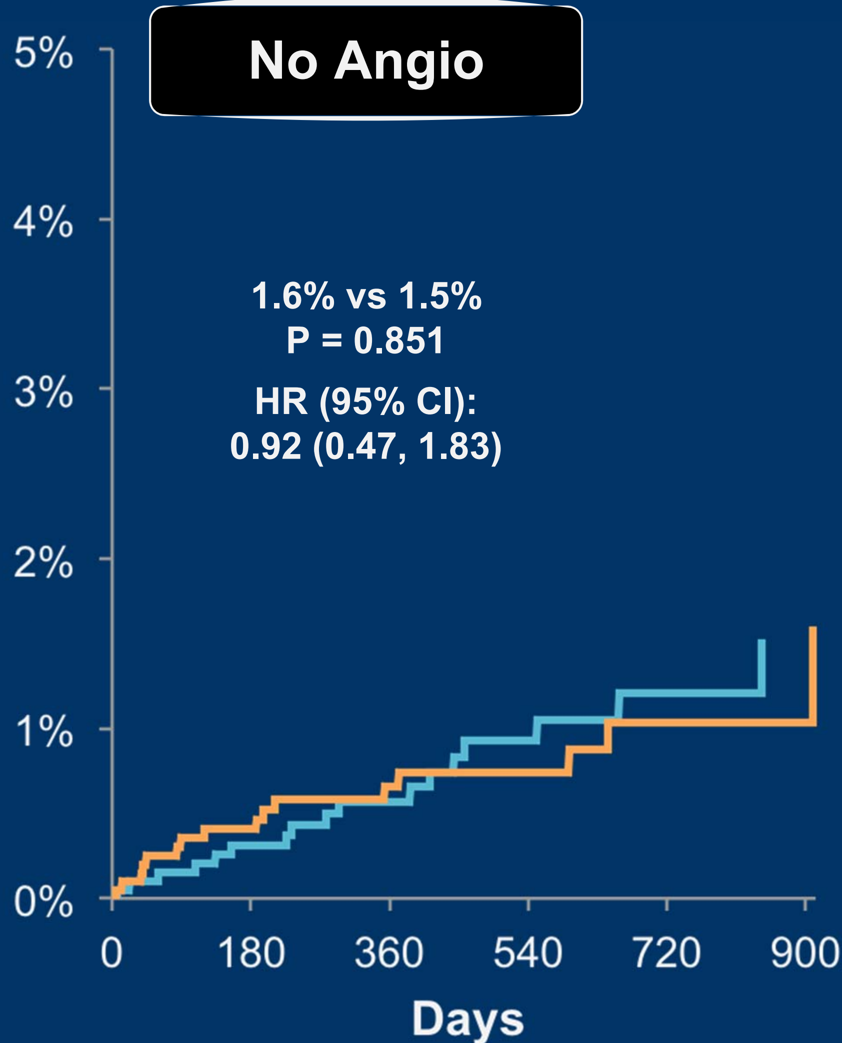
P interaction = 0.12

TIMI Major Bleeding

TRILOGY ACS

Prasugrel — Clopidogrel





P interaction = 0.16

Conclusions

- Substantial differences exist among patients triaged for medical therapy with or without angiography from TRILOGY ACS.
  - Geographically, subjects from North America, Western Europe, and the Mediterranean tended to have angiography pre-randomization
  - Patients with angiography more often were enrolled with NSTEMI, and had prior history or PCI or CABG
- Patients with angiography had lower overall events rates, particularly CV death.

Conclusions

- Overall, in the TRILOGY ACS Trial prasugrel did not reduce cardiovascular events among patients managed medically for ACS.
- When treated with prasugrel compared to clopidogrel, patients triaged to medical therapy following angiography tended to have:
    - lower rates of the combined endpoint of CVD/MI/CVA
    - Lower rates of MI, CVA alone, and recurrent ischemic events
    - higher rates of bleeding.
- Though hypothesis generating, these results are consistent with previous trials and suggest when angiography is performed and coronary disease is confirmed, the benefits and risks of intensive antiplatelet therapy exist whether medical therapy or PCI is elected.