

#AHA23

CAD POLYGENIC RISK SCORE AND INCIDENT COMPLEX CORONARY REVASCULARIZATION IN ADULTS WITH ATHEROSCLEROSIS

Sachit Singal, MD,¹ Frederick K. Kamanu, PhD, Giorgio Melloni, PhD,
Carolina Roselli, MSc, Robert P. Giugliano, MD, ScM, Patrick T.
Ellinor, MD, PhD, Marc S. Sabatine, MD, MPH, Christian T. Ruff, MD,
MPH, Nicholas A. Marston, MD, MPH, Brian Bergmark, MD

¹Department of Medicine, Brigham and Women's Hospital, Harvard Medical
School, Boston, MA, USA



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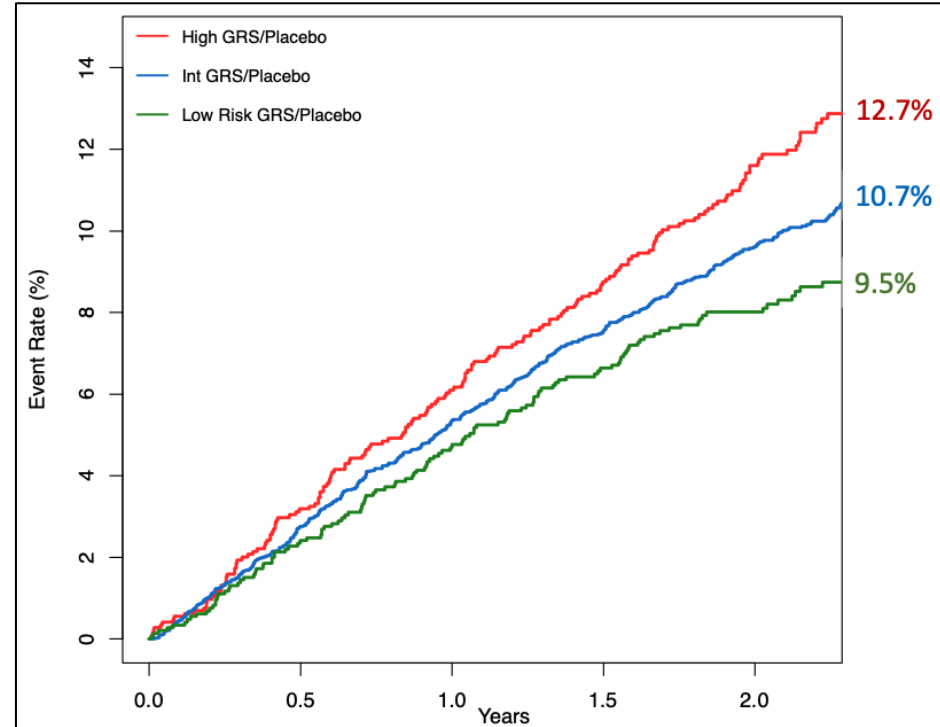
DISCLOSURES

Drs. Bergmark, Marston, Ruff, Sabatine, and Giugliano are members of the TIMI Study Group, which has received institutional research grant support through Brigham and Women's Hospital from Abbott, Abiomed, Inc., Amgen, Anthos Therapeutics, ARCA Biopharma, Inc., AstraZeneca, Boehringer Ingelheim, Daiichi-Sankyo, Ionis Pharmaceuticals, Inc., Janssen Research and Development, LLC, MedImmune, Merck, Novartis, Pfizer, Regeneron Pharmaceuticals, Inc., Roche, Saghmos Therapeutics, Inc., Siemens Healthcare Diagnostics, Inc., Softcell Medical Limited, The Medicines Company, Verve Therapeutics, Inc., and Zora Biosciences.

INTRODUCTION

Coronary Artery Disease Polygenic Risk Score (CAD PRS)

- Previously shown to predict major vascular events among patients with established ASCVD
 - Major Coronary Events
 - Ischemic stroke



Marston NA et al. *Circulation*. 2020;141:616–623

OBJECTIVE

To investigate whether the CAD PRS can predict incident complex coronary revascularization events in patients with established ASCVD enrolled in the FOURIER trial

METHODS

- Prospective genetic cohort analysis of 14,298 patients from **The FOURIER Trial**
- CAD PRS from a CAD genome-wide association study (2,293,205 SNPs)
- Complex revascularization
 - Complex PCI (as defined by the GLOBAL LEADERS trial): ≥ 1 of multivessel PCI, ≥ 3 stents, ≥ 3 lesions treated, bifurcation PCI, or total stent length >60 mm¹
 - CABG
- Associations between CAD PRS and revascularization events analyzed by quintile

¹Serruys PW et al. *Euro Heart J.* 2019;40:2595–2604

METHODS

- CAD PRS was categorized by quintile:
 - **Low risk (Q1):** $\leq 20^{\text{th}}$ percentile
 - **Intermediate Risk (Q2-Q4):** $>20^{\text{th}}$ and $<80^{\text{th}}$ percentile
 - **High Risk (Q5):** $\geq 80^{\text{th}}$ percentile
- Differences in overall complex revascularization, complex PCI, CABG, and individual components of complex PCI compared using a Cox proportional hazards model

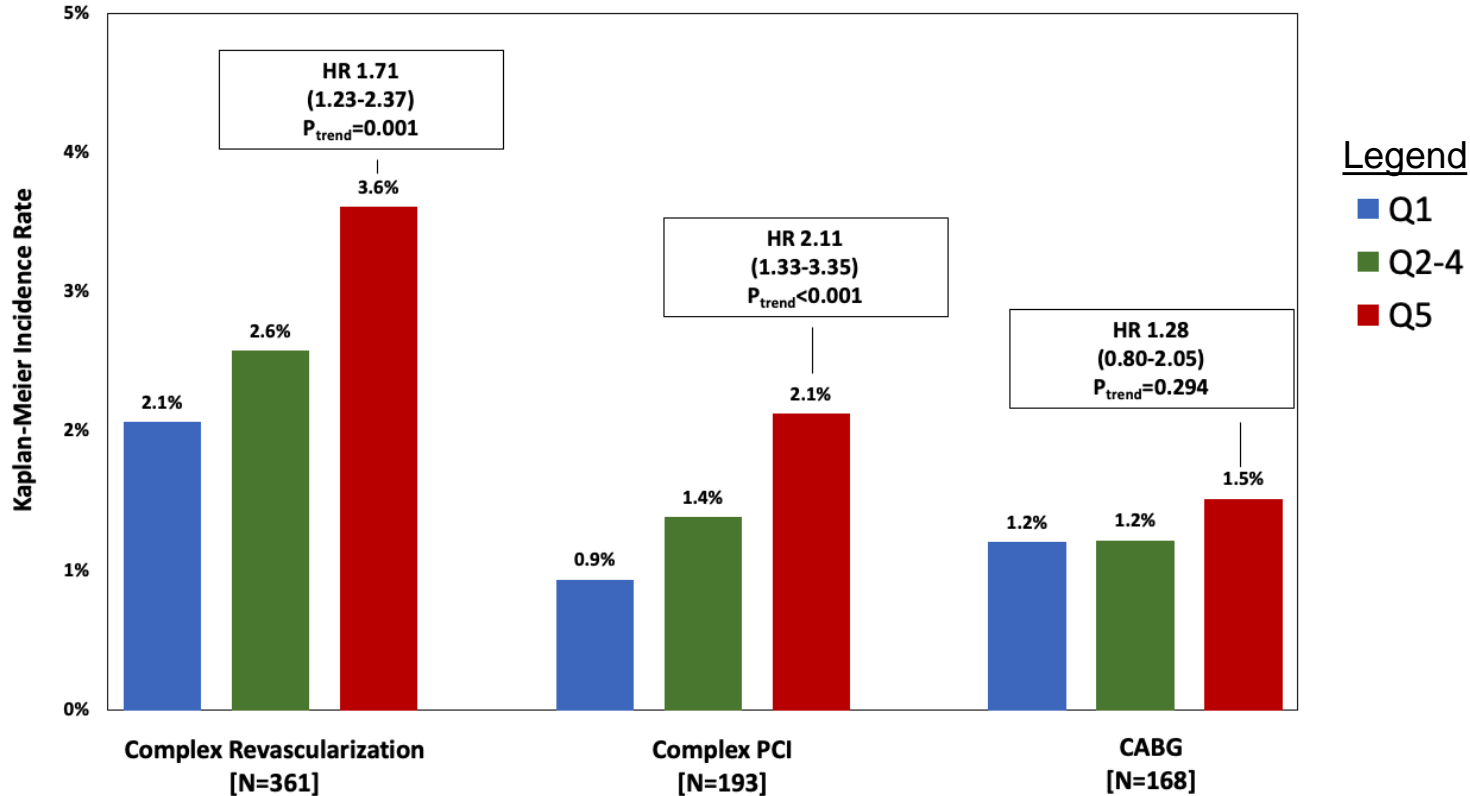
RESULTS

Baseline Characteristics of Study Population

Variable	Low Risk N=2864	Intermediate Risk N=8574	High Risk N=2860
Age, yrs	64 (8)	63 (8)	61 (8)
Male Sex	77%	77%	73%
BMI, kg/m ²	29 [26, 32]	29 [26, 32]	29 [26, 32]
Diabetes	32%	32%	31%
Hypertension	78%	81%	81%
LDL-C (mg/dL)	91 [79, 108]	93 [80, 109]	93 [81, 110]

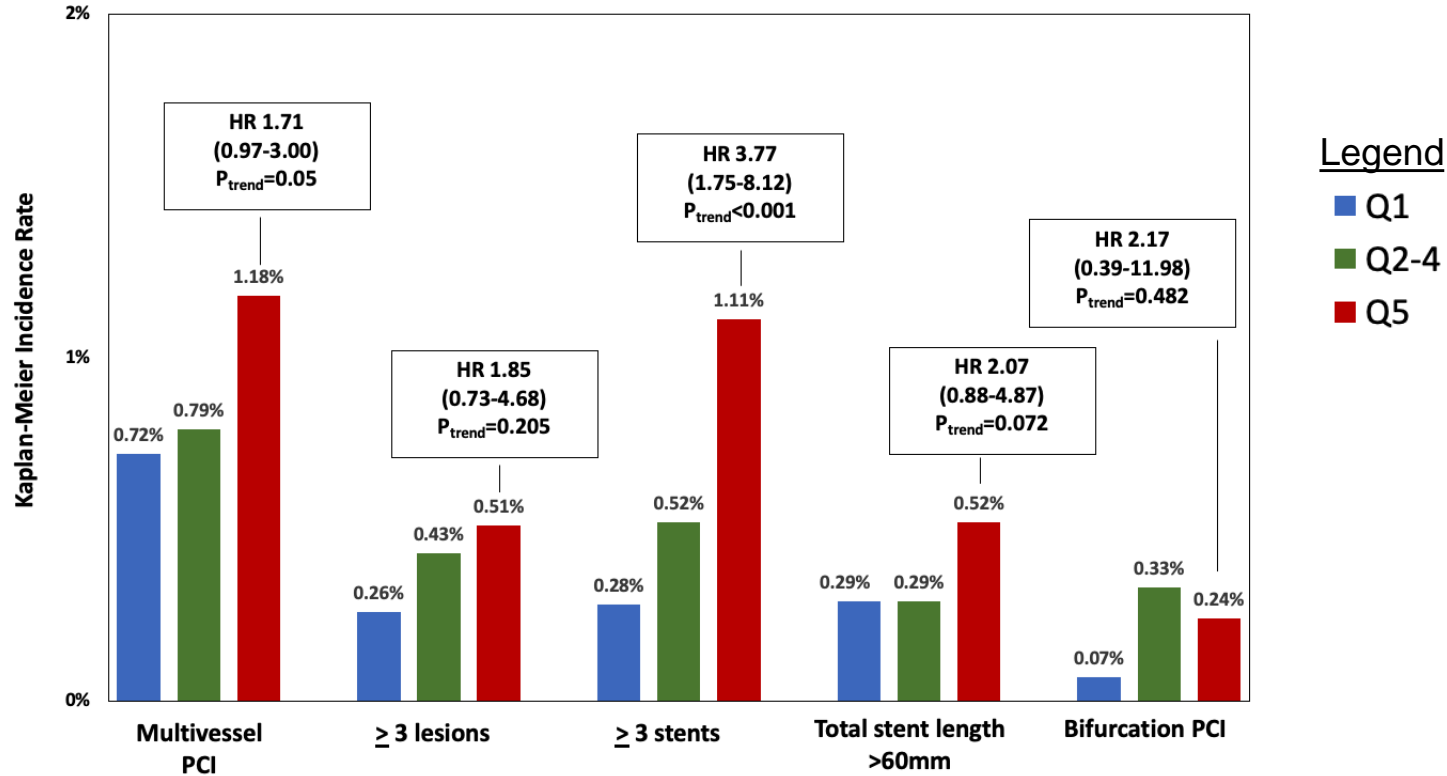
RESULTS

Complex Revascularization Outcomes by CAD PRS



RESULTS

Outcomes by Individual Components of Complex PCI



LIMITATIONS

- **Details of individual patient coronary anatomy at baseline were not available**
- **Despite a large sample size, the numbers of events for specific components of complex PCI were small, limiting the power to detect differences between groups**

CONCLUSION

- **Among patients with established ASCVD, CAD PRS was associated with incident complex coronary revascularization procedures**
- **Polygenic risk stratification may promote opportunities for targeted prevention in select patients (with the goal of ultimately reducing the need for high-risk and costly procedures)**

THANK YOU



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