



Sex-Based Differences in Outcomes Following Peripheral Artery Revascularization: Insights from VOYAGER PAD

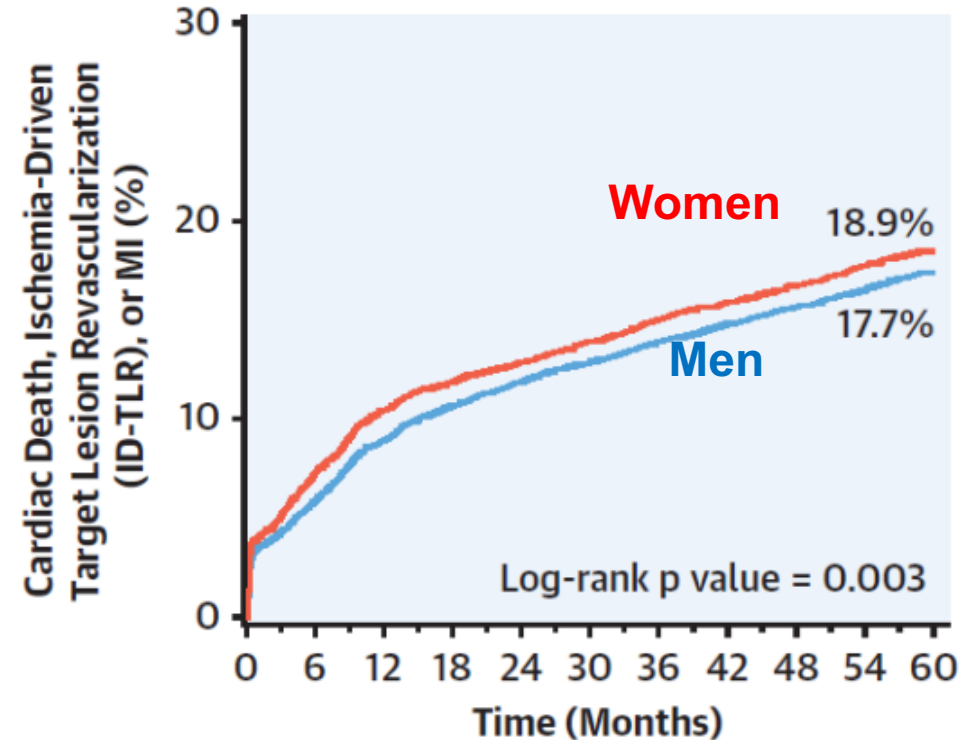
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*European Society of Cardiology Congress 2021
Late-Breaking Science
26 August 2021*

Peripheral Artery Disease in Women

- >200 million people w/ PAD globally
- Patients with PAD are at high risk of major adverse cardiovascular events and major adverse limb events
 - Dominant morbidity in PAD related to limb outcomes, including lower extremity revascularization (LER)
- Prevalence of PAD in women as high or higher than in men
- Coronary studies suggest outcomes may differ on the basis of sex

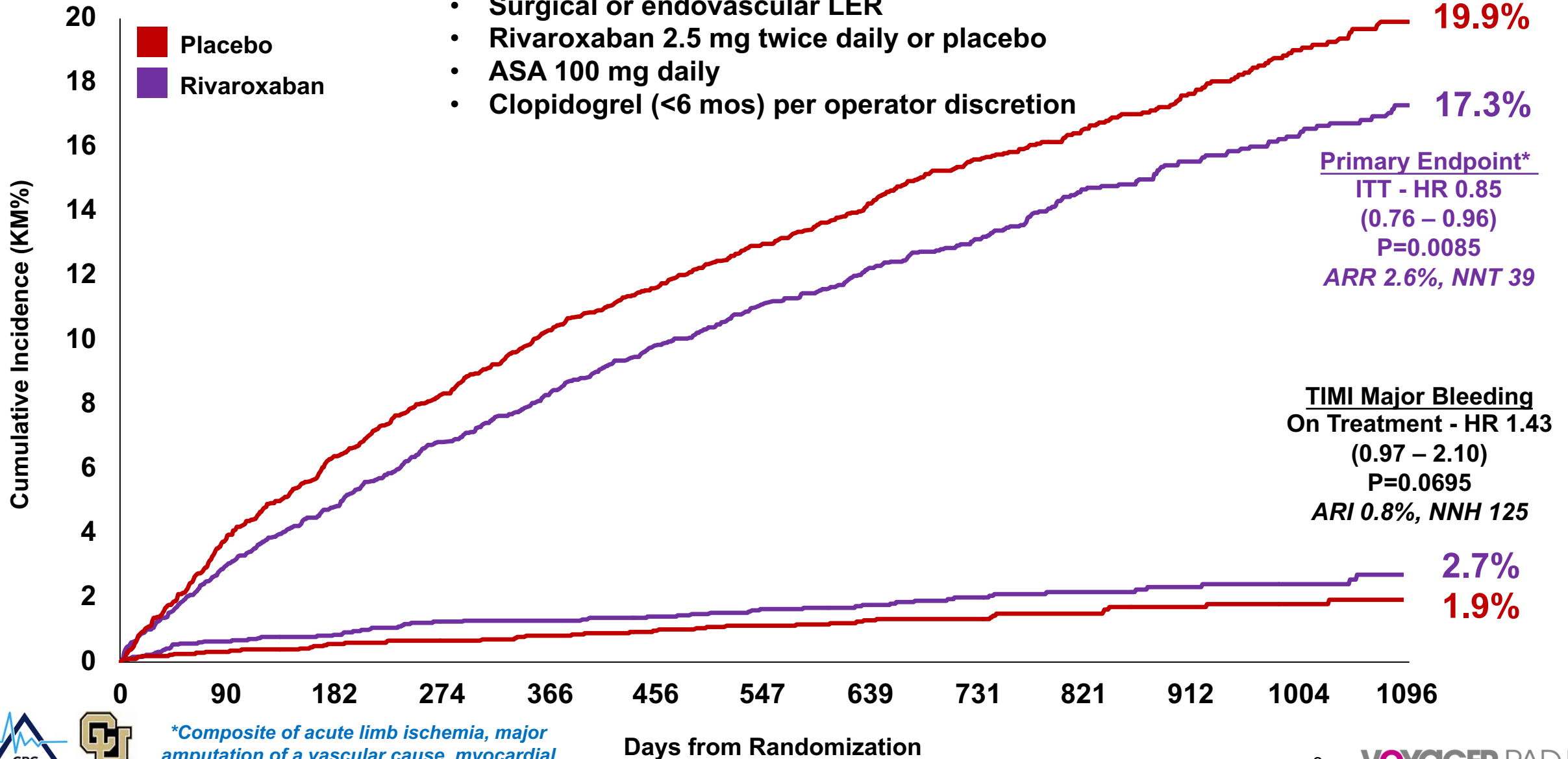
Outcomes after Percutaneous Coronary Intervention by Sex



Risk profile and outcomes after LER in women w/ symptomatic PAD are not well understood

VOYAGER PAD Primary Results

- 6,564 symptomatic PAD patients
- Surgical or endovascular LER
- Rivaroxaban 2.5 mg twice daily or placebo
- ASA 100 mg daily
- Clopidogrel (<6 mos) per operator discretion



*Composite of acute limb ischemia, major amputation of a vascular cause, myocardial infarction, ischemic stroke, cardiovascular death



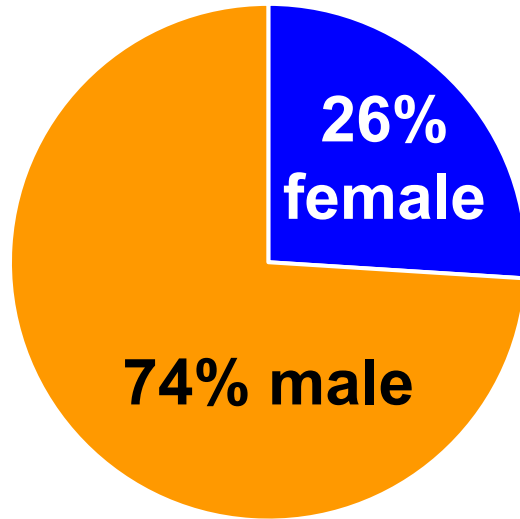
Objectives and Methods

- **To examine sex-based differences in:**
 - **Trial metrics (recruitment and adherence)**
 - **Cardiovascular and limb outcomes**
 - **Efficacy and safety of rivaroxaban**
- **Prespecified subgroup analysis of VOYAGER PAD**
- **Outcomes prospectively ascertained and independently adjudicated by a blinded committee**
- **Associations between sex and outcomes and effects of rivaroxaban estimated with adjusted Cox proportional hazards models**
 - **Intention-to-treat and on-treatment analyses performed**

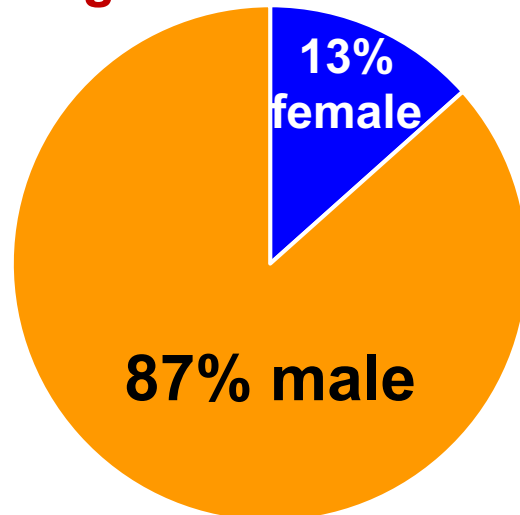
Female Participation in VOYAGER PAD

6,564 patients enrolled at 542 sites in 34 countries

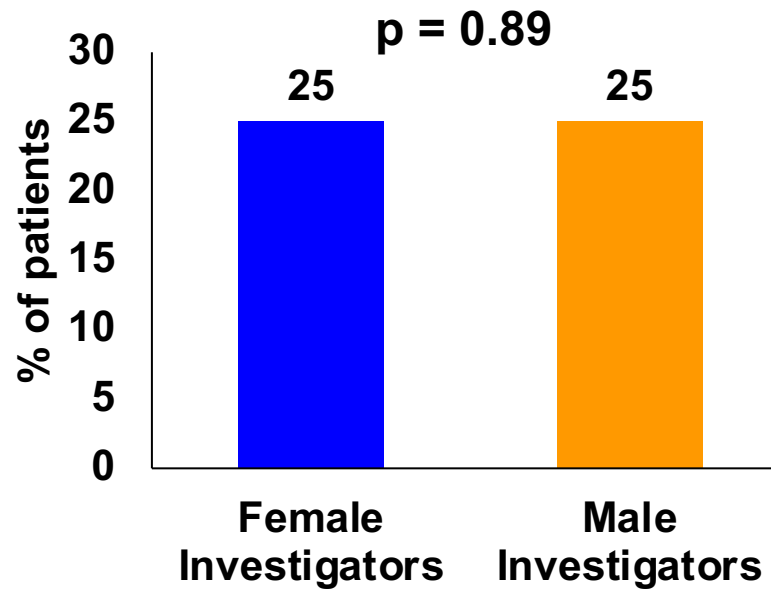
Subjects Enrolled



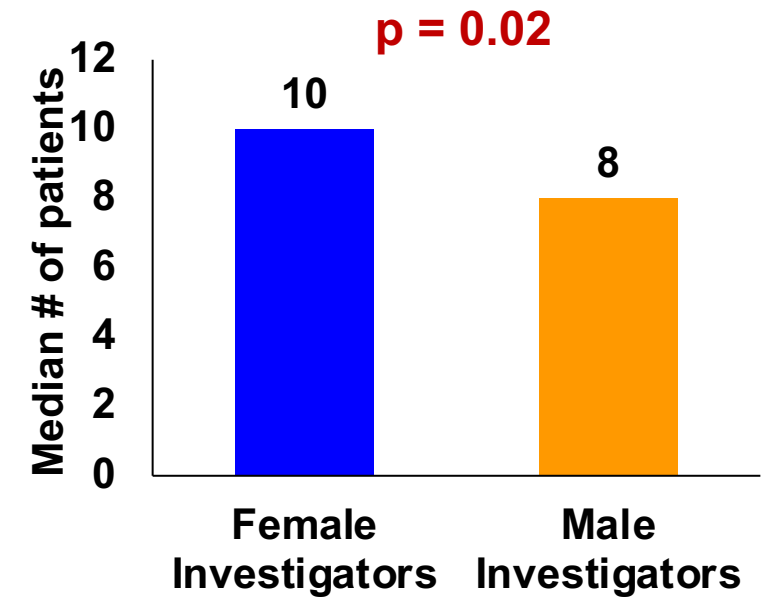
Site Investigators



Female enrollment



Overall enrollment



Baseline Characteristics

Characteristic at Randomization	Women N=1704 %	Men N=4860 %	P-value
Age, years median (IQR)	69 (63-76)	66 (60-72)	<0.0001
BMI, kg/m², median (IQR)	26 (23-29)	26 (24-29)	NS
Caucasian	80	81	NS
Hypertension	86	80	<0.0001
Diabetes mellitus	42	41	NS
Hyperlipidemia	63	59	0.005
eGFR < 60 ml/min/1.73m²	30	17	<0.0001
Current smoking	26	38	<0.0001
Coronary artery disease	27	33	<0.0001
Baseline clopidogrel use	55	49	<0.0001
Baseline statin use	80	80	NS

PAD & Procedural Characteristics

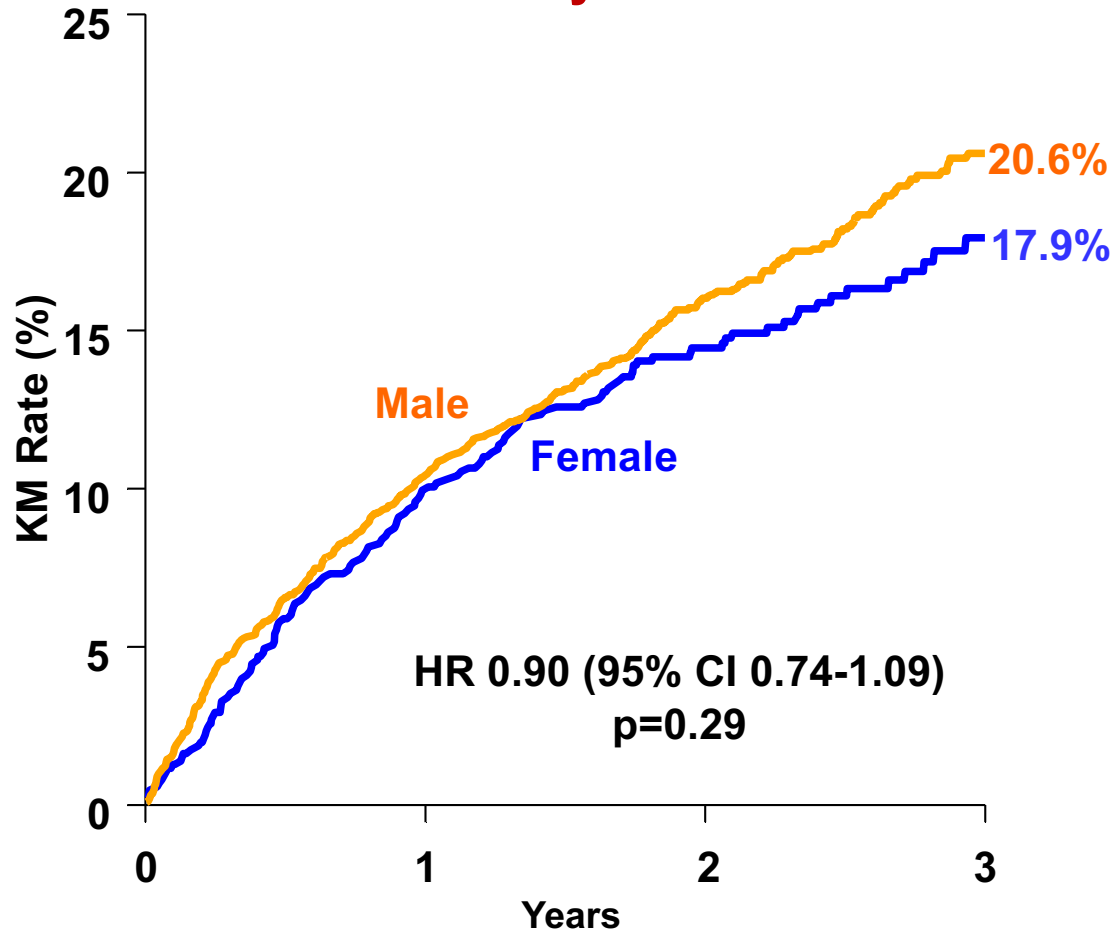
	Women N= 1704 %	Men N= 4860 %	P-value
<i>Peripheral Artery Disease History</i>			
Prior lower extremity revascularization	35	36	NS
Prior amputation	5	6	NS
Baseline ABI ≤0.50	40	41	NS
<i>Index Revascularization</i>			
Performed for critical limb ischemia	26	23	0.006
Long (≥15 cm) target lesion	33	35	NS
Endovascular (including hybrid)	74	64	<0.0001
Atherectomy*	9.1	6.3	0.002
Drug-coated device*	31	31	NS

NS = not significant

*among patients undergoing endovascular revascularization

Outcomes in Placebo Patients by Sex

Primary outcome



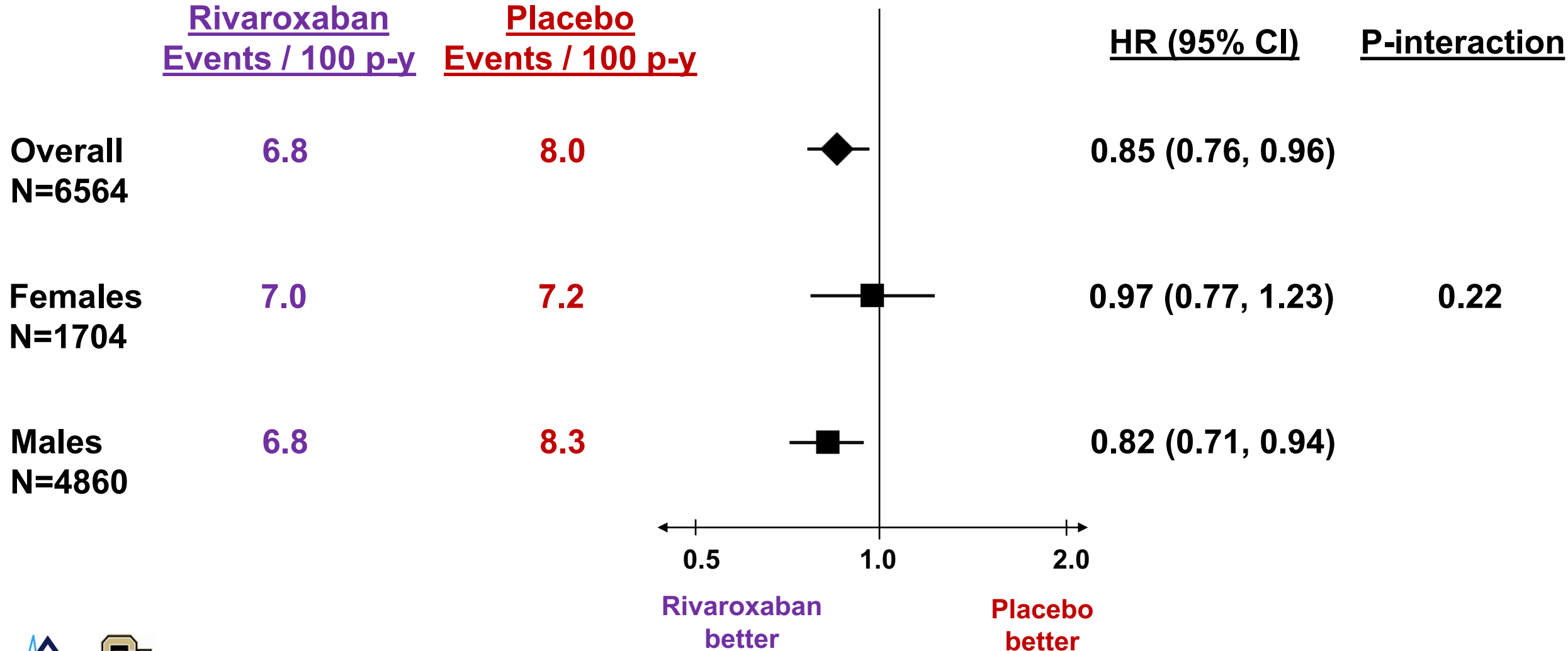
Number at Risk

Female	857	756	577	180
Male	2421	2126	1576	468

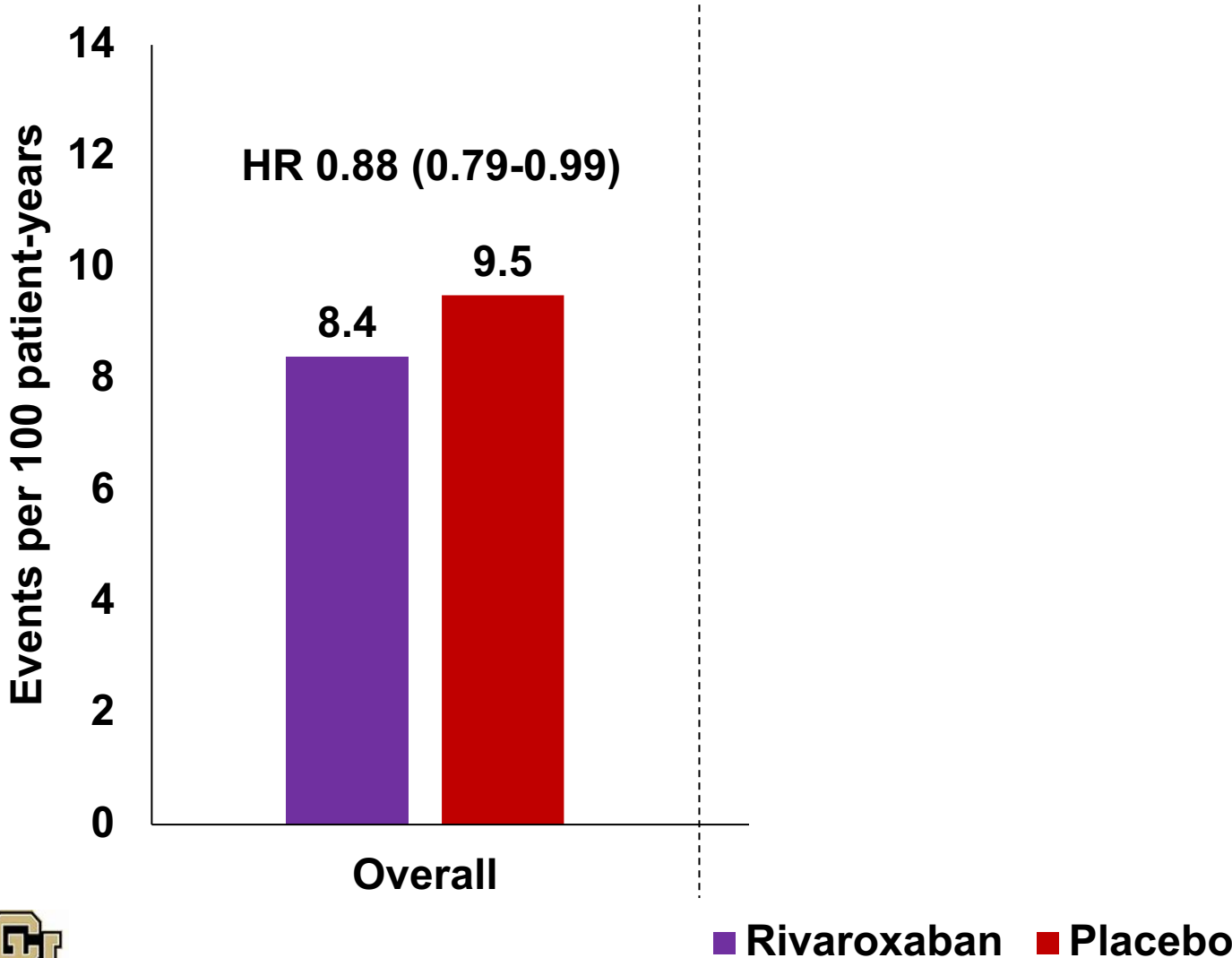
HR reflects stratification for endovascular vs surgical index revascularization

*Additionally adjusted for age, BMI, hypertension, hyperlipidemia, diabetes, CAD, eGFR<60 ml/min/1.73m², current smoking

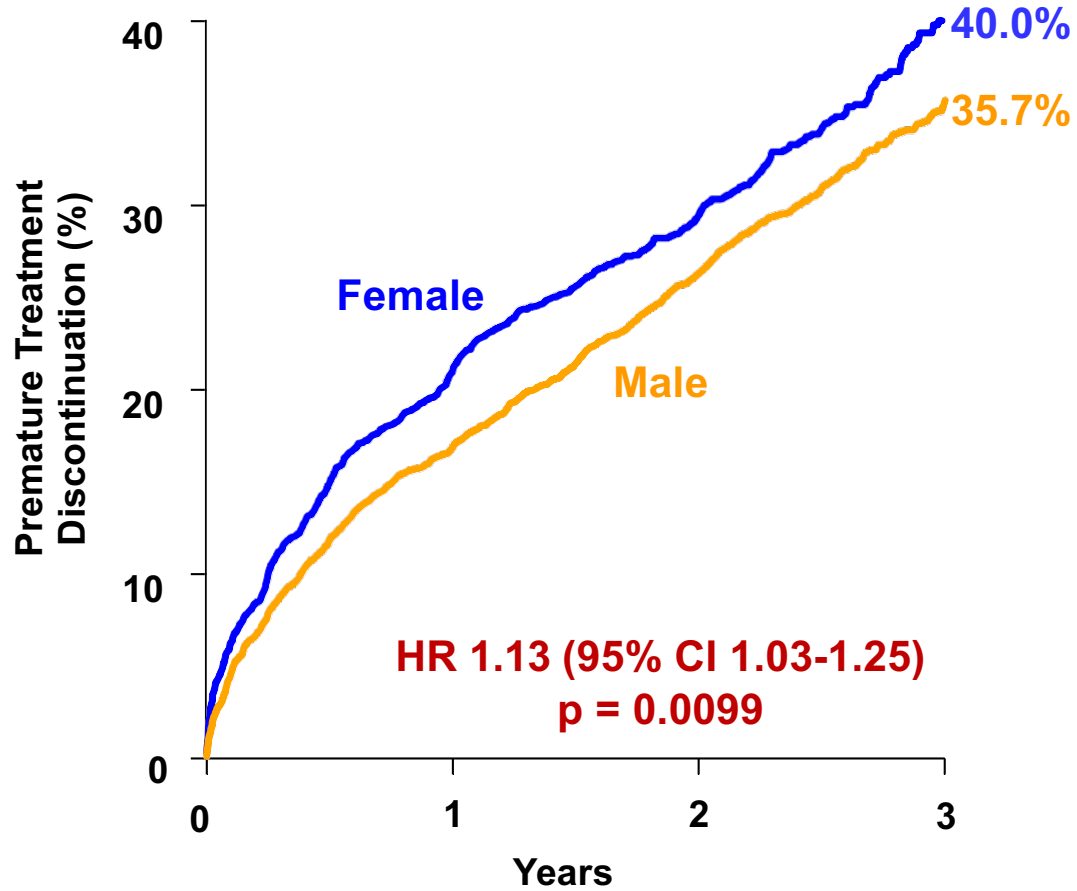
Effect of Rivaroxaban on the Primary Outcome by Sex (Intention-to-Treat)



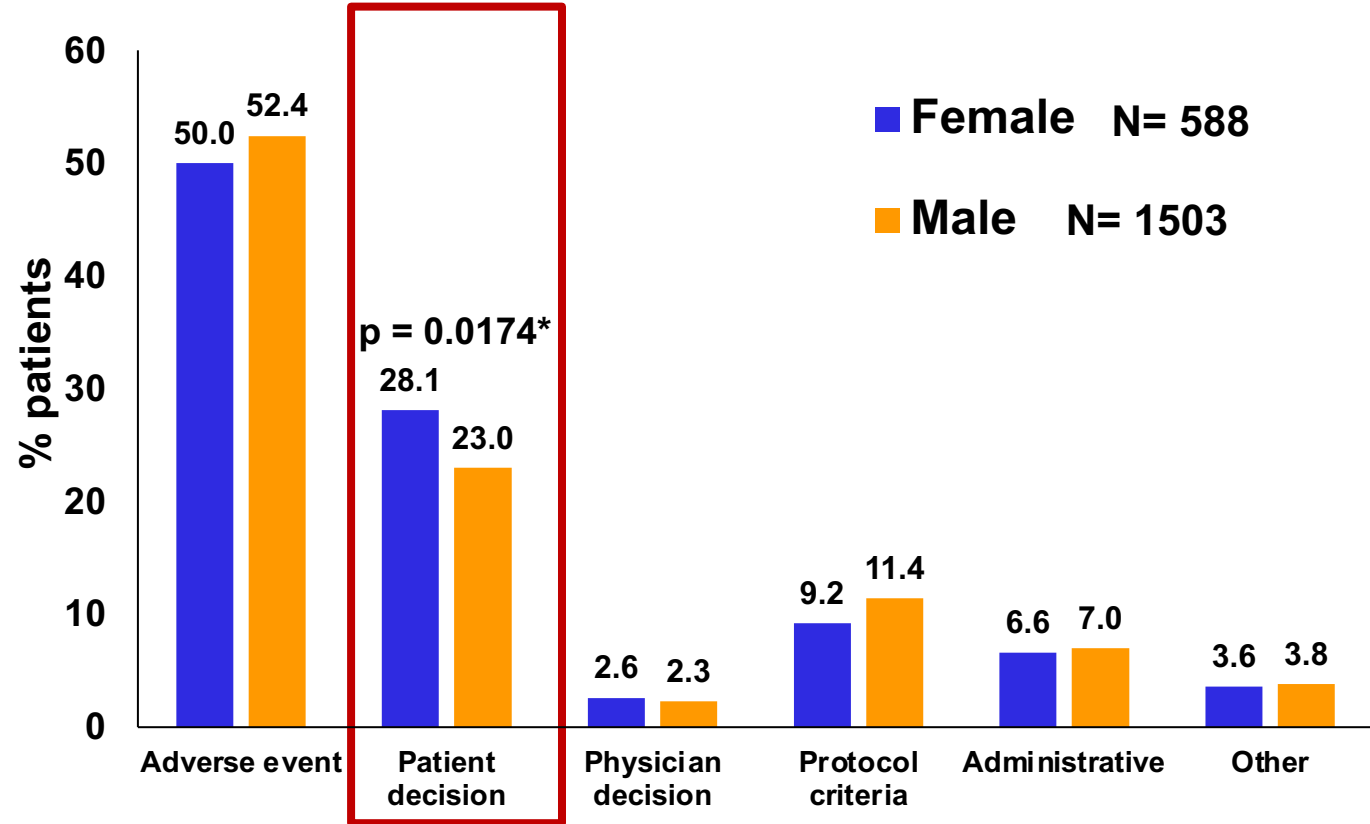
Effect of Rivaroxaban on Unplanned Index Limb Revascularization by Sex



Women More Frequently Discontinued Study Medication



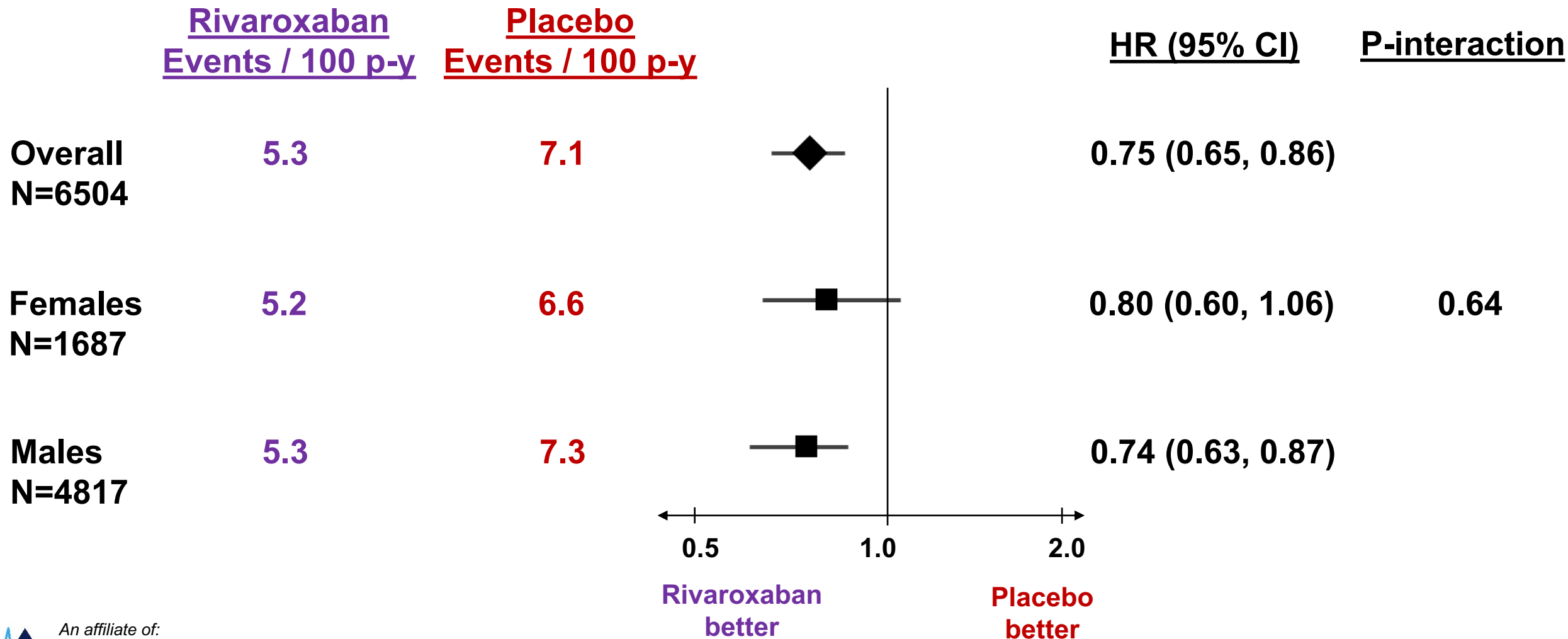
Reasons for treatment discontinuation



Pattern of d/c (rivaroxaban or placebo) similar for females and males

D/C at sites with female PIs 29.4% versus male PIs 32.7% (p=0.0375)

Effect of Rivaroxaban on the Primary Outcome by Sex (On-Treatment)

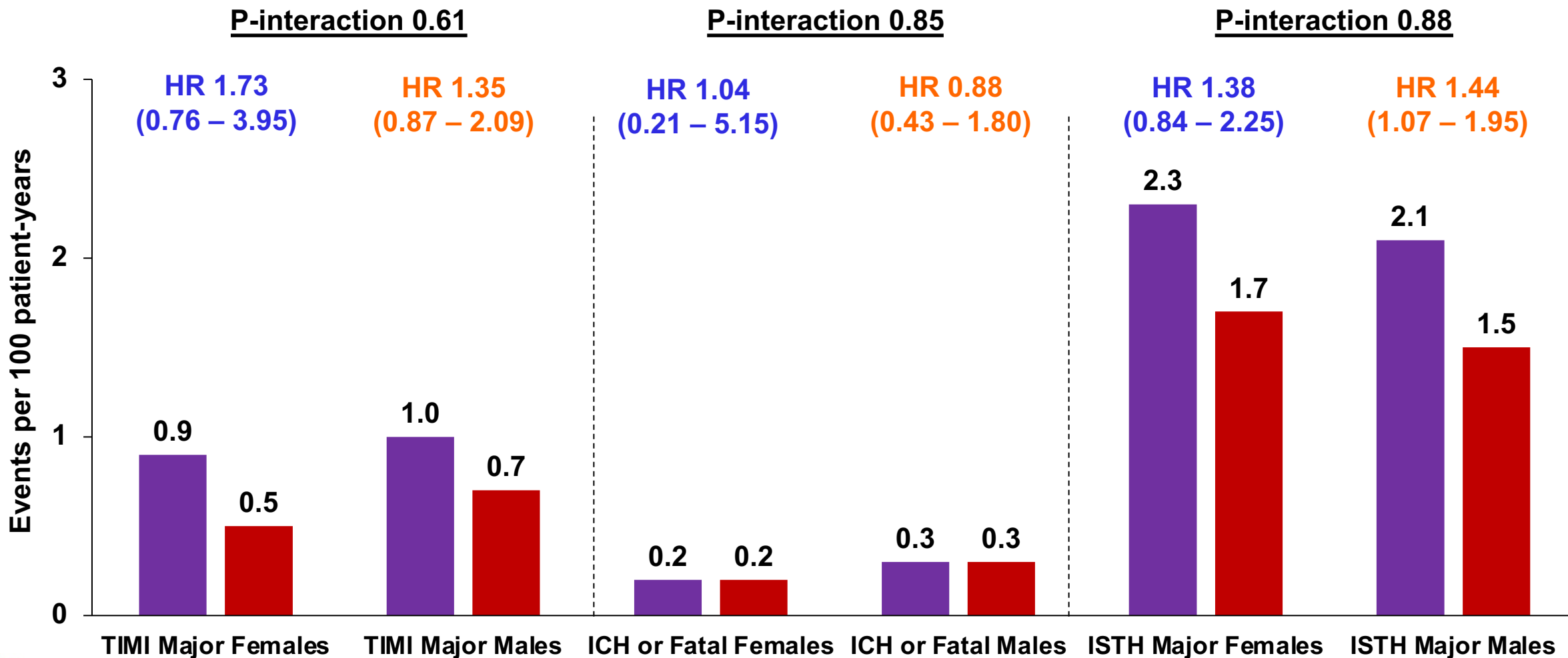


Safety of Rivaroxaban by Sex

■ Placebo
■ Rivaroxaban

Females
 N=1,687

Males
 N=4,817



Summary and Conclusions

- **>1,700 women in VOYAGER PAD → one of the largest experiences of post-LER outcomes in women**
 - **~1/4 of patients female**
- **Compared with men, women were enriched for risk factors, presented with more severe PAD, underwent more endovascular LER, and had greater risk of unplanned index limb revascularization**
- **Efficacy and safety of rivaroxaban were consistent irrespective of sex**
 - **Study treatment discontinuation more common in women than men**
- **Efforts to understand sex-based differences in outcomes after LER and clinical trial participation and treatment adherence are needed**
 - **Prospective data collection and studies on the impact of women in site and leadership roles**