



VIII CONGRESSO
NAZIONALE
PIEDE DIABETICO
INTERASSOCIATIVO SID-AMD

Focus sul piede nella
gestione del diabete

ROMA, 18-20 GIUGNO 2026

HOTEL NH VILLA CARPEGNA

La terapia «medica» nell'ischemia «critica» d'arto

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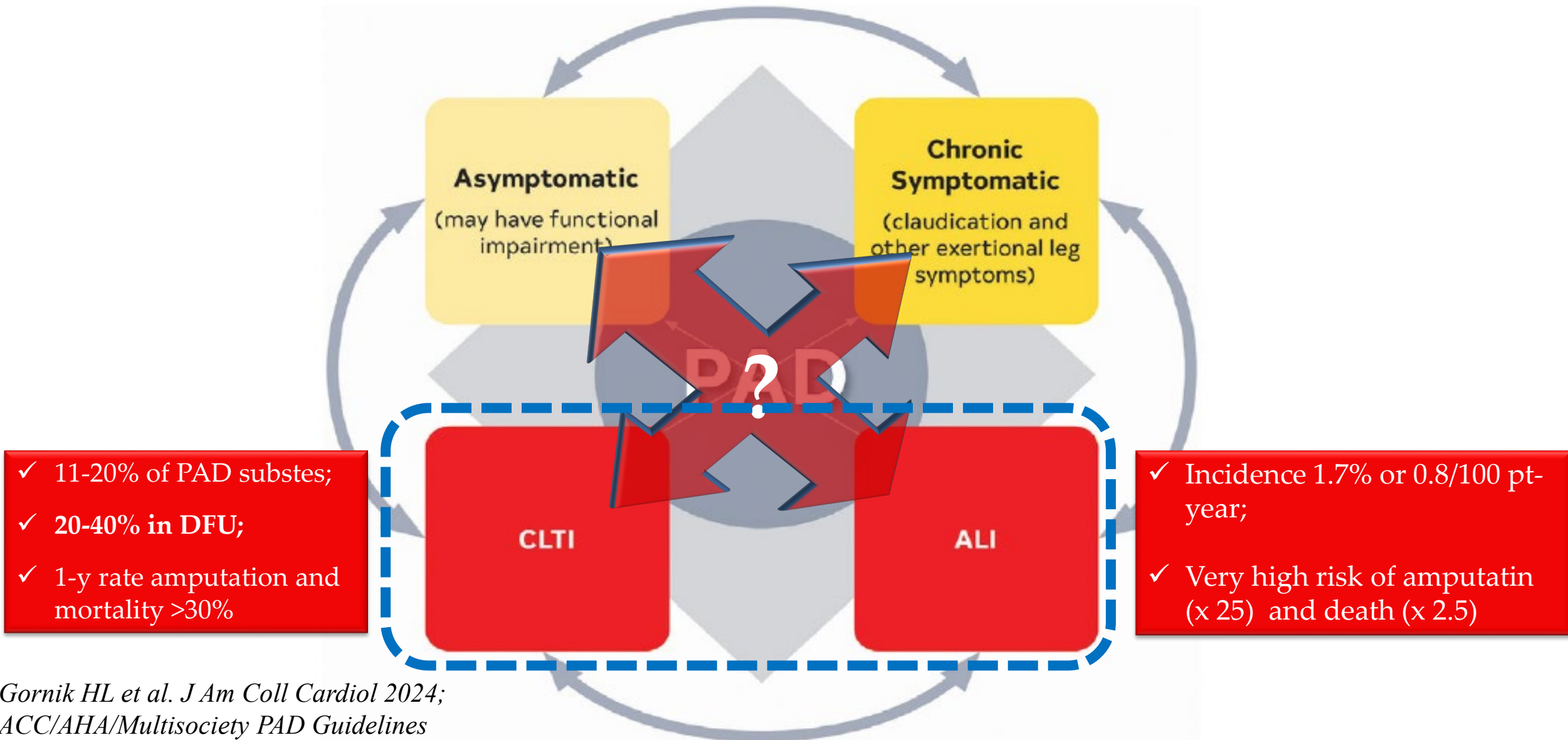
Disclosures

Il sottoscritto Dr. Giuseppe Murdolo dichiara di non aver ricevuto negli ultimi due anni compensi o finanziamenti da Aziende Farmaceutiche e/o Diagnostiche

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Clinical Subsets of PAD



The PAD “Dogma”:

moving away the “athero-centric” view

The “athero-centric” view

- ✓ *“Peripheral arterial disease leading to stenosis or occlusion of arteries supplying the lower limbs caused by **atherosclerosis** in ~ 95% of cases”;*
- ✓ *“Lower extremity PAD can be defined as **obstructive atherosclerotic disease** of the arteries from the distal aorta to the foot resulting in disturbed or impaired circulation to one or both lower extremities”;*
- ✓ *“CLTI is an **end-stage manifestation of systemic atherosclerosis**”*

Pathological Characterization of Peripheral Arteries in Amputations for Critical Limb Ischemia



Thrombotic luminal occlusion with insignificant atherosclerosis and abundance of medial calcification suggest a different pathophysiologic phenotype of “diabetic” PAD: a challenge to the traditional “athero-centric” view

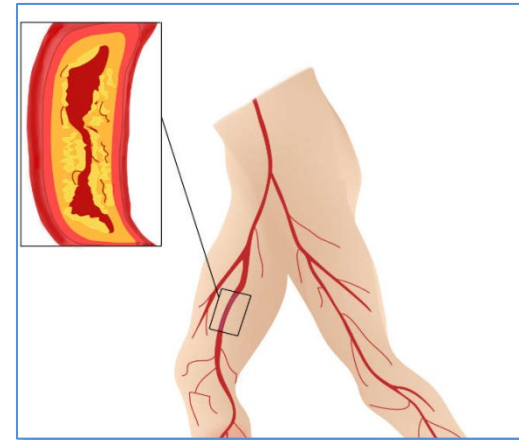
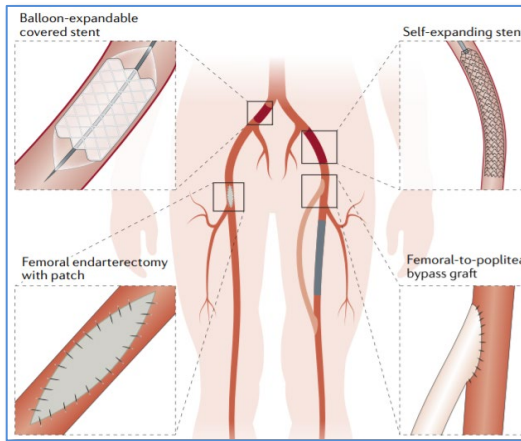
MAC-related thrombi

FA: fibroatheroma; FC: fibrocalcific plaque

Terapia con DPI nel “continuum” vascolare: *dal setting “cronico” alla fase critica “post-rivascolarizzazione”*

Post-revascularisation

Chronic phase



COMPASS 

MACE ↓ 24%
Mortalità CV ↓ 22%
Stroke ↓ 42%
MALE ↓ 46%
Maj. Amput ↓ 70%
ALI ↓ 44%
CLTI ↓ 33%

ORIGINAL ARTICLE

Rivaroxaban in Peripheral Artery Disease after Revascularization

Marc P. Bonaca, M.D., M.P.H., Rupert M. Bauersachs, M.D.,
Sonia S. Anand, M.D., E. Sebastian Debus, M.D., Ph.D., Mark R. Nehler, M.D.,
Manesh R. Patel, M.D., Fabrizio Fanelli, M.D., Warren H. Capell, M.D.,
Lihong Diao, M.D., Nicole Jaeger, M.S., Connie N. Hess, M.D., M.H.S.,
Akos F. Pap, M.Sc., John M. Kittelson, Ph.D., Ivan Gudz, M.D., Ph.D.,
Lajos Mátyás, M.D., Dainis K. Krievins, M.D., Rafael Diaz, M.D.,
Marianne Brodmann, M.D., Eva Muehlhofer, M.D., Lloyd P. Haskell, M.D.,
Scott D. Berkowitz, M.D., and William R. Hiatt, M.D.

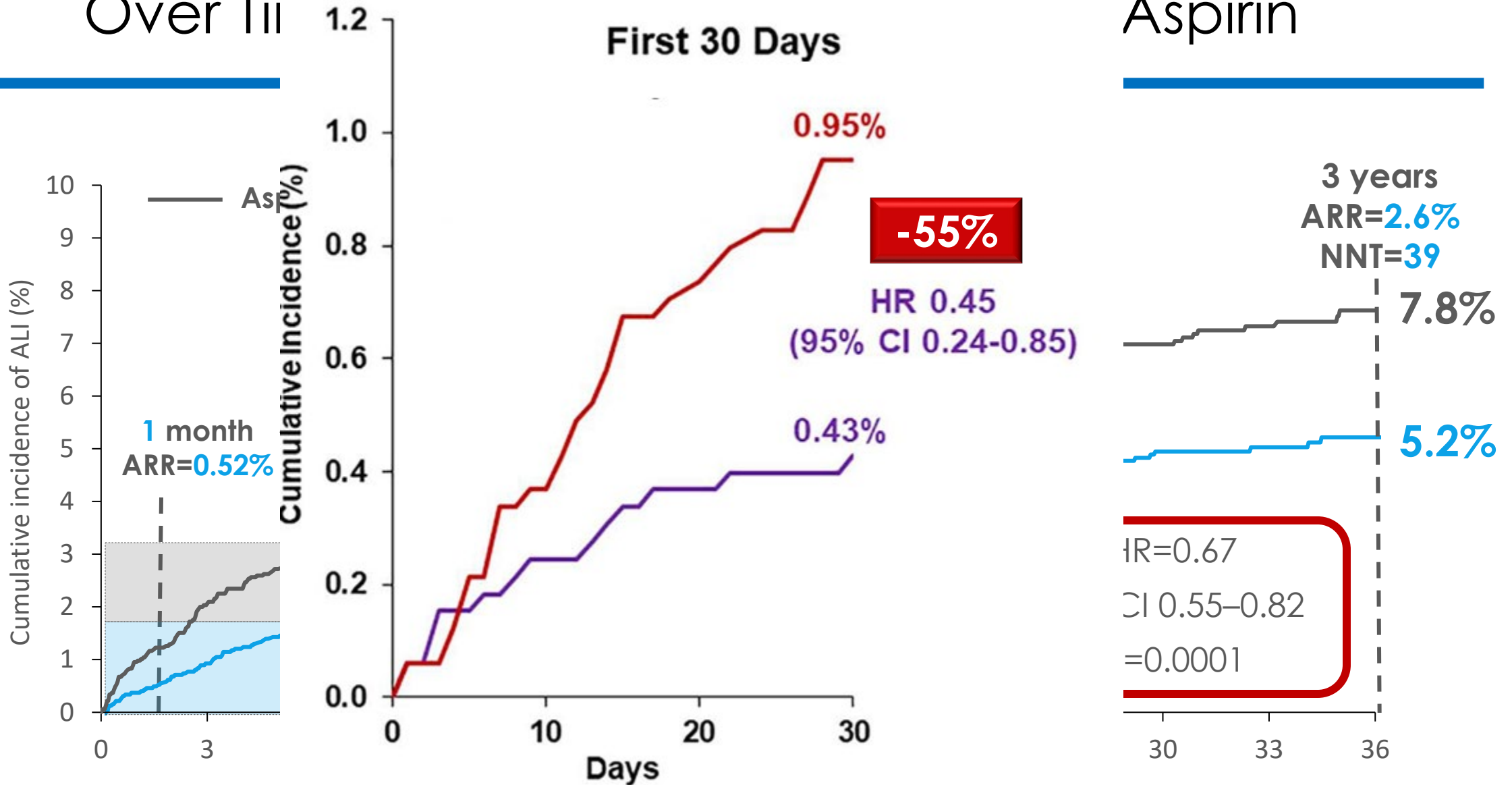
Baseline Characteristics

Characteristics at Randomization	Rivaroxaban 2.5 mg twice daily + aspirin N=3286 %	Placebo + aspirin N=3278 %
Age, Yrs Median	67	67
Female	26	26
Caucasian	81	81
Diabetes Mellitus	40 (1314)	40 (1311)
Clopidogrel	51 (1676)	51 (1672)
Statin	79	81
ACEi or ARB	64	63
<i>Indication for Revascularization</i>		
Critical limb ischemia	23 (766)	24 (787)
Claudication	77	76

P>0.05 for all

1 paziente su 2 riceveva una DAPT (ASA + Clopidogrel) al momento dell'arruolamento

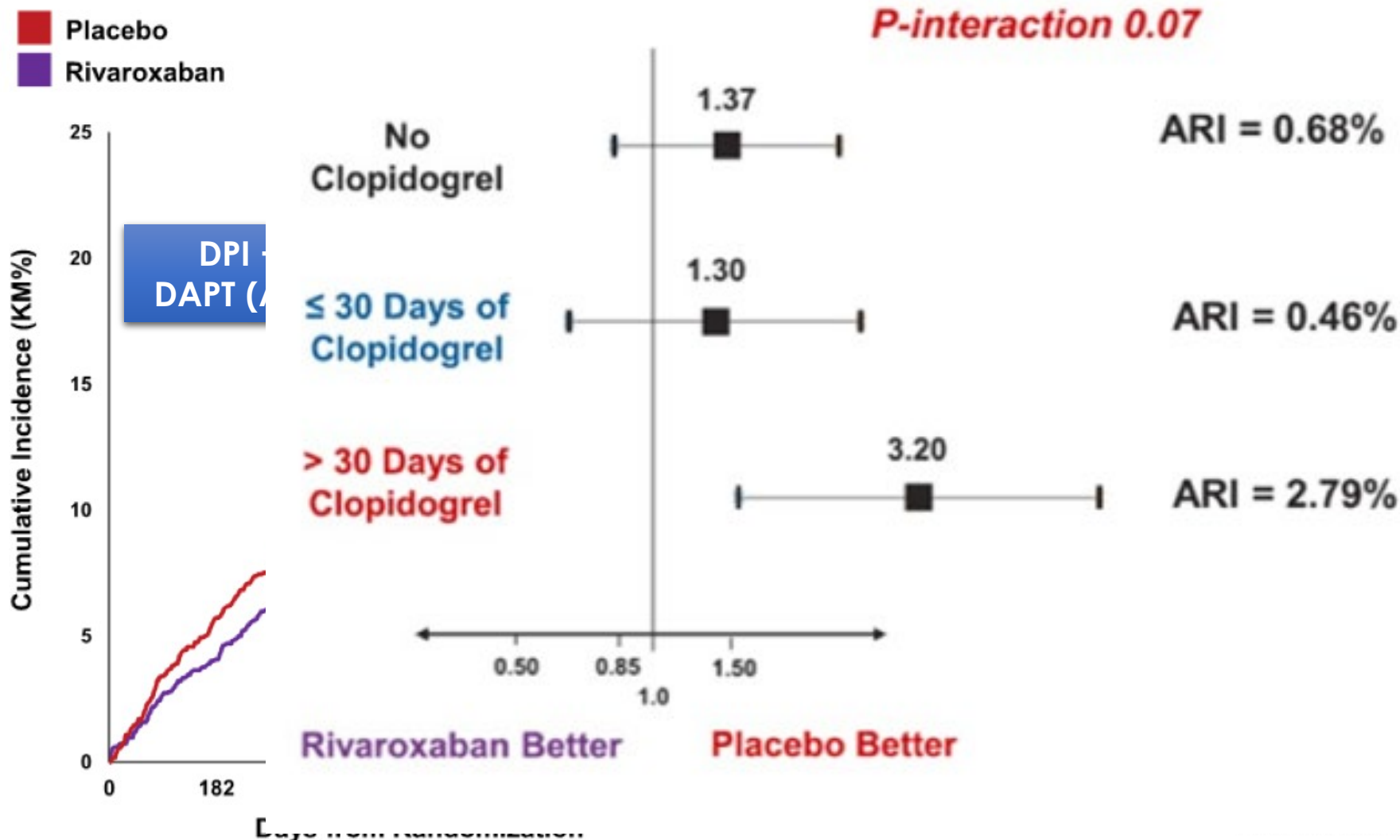
Patients Treated with DPI Experienced Fewer ALI Events Over Time Compared to Aspirin



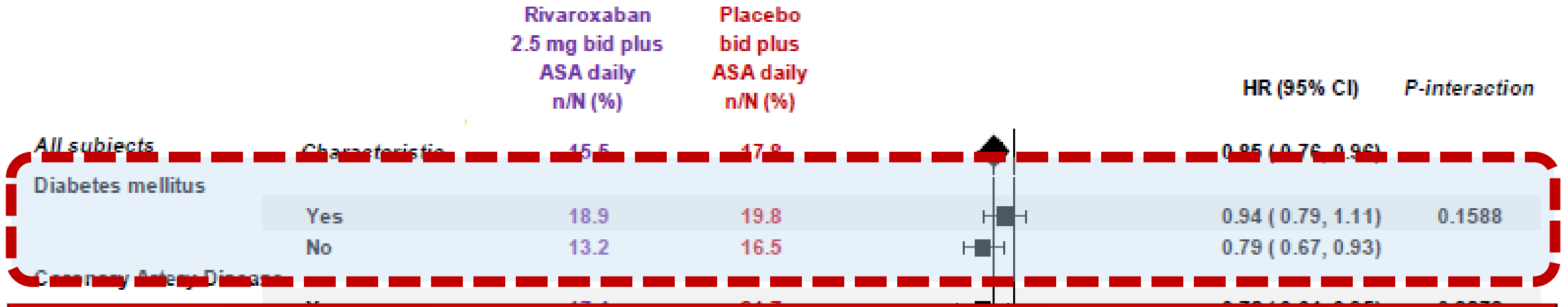
Impact of Results From

ISTH Major Bleeding

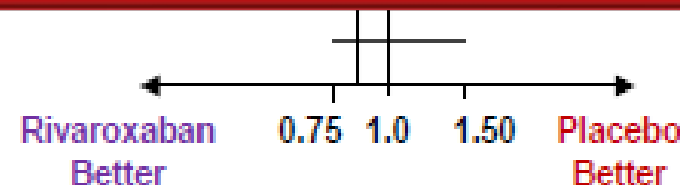
point



Primary Efficacy Outcome in Selected Subgroups



*Was the diabetic patient with CLTI really represented in
the VOYAGER-PAD ?*



Effects of DPI in Fragile Patients with PAD Who Underwent LER From the VOYAGER PAD Trial



41% Female

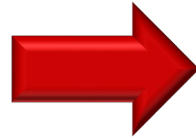
Fragile Patients

- Age >75 years
- CKD
- Low BMI



59% Male

1674/6564
(25%)



Very High CV Risk

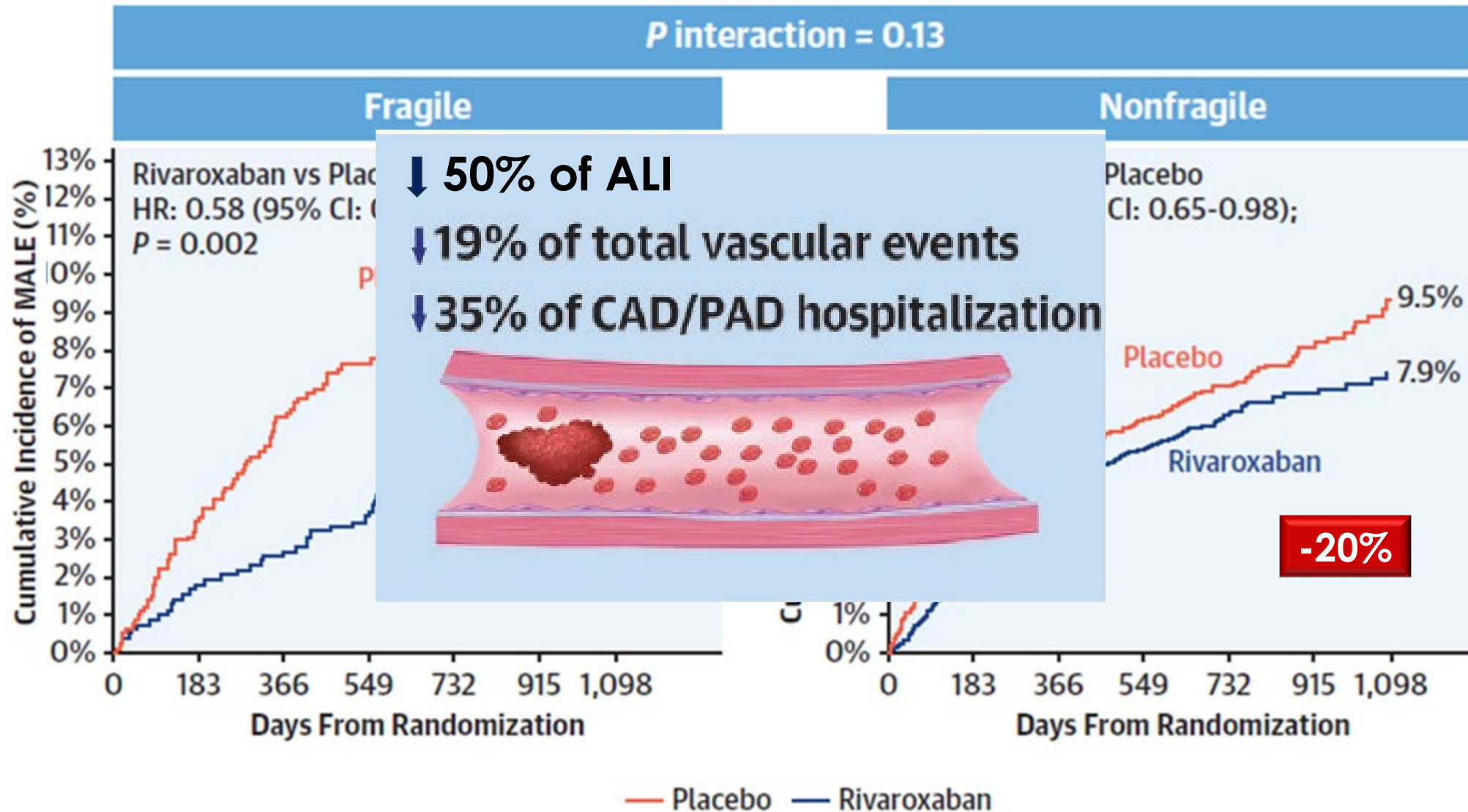
- 88% Arterial hypertension
- 59% Hyperlipidemia
- 45% Diabetes mellitus
- 36% CAD
- 34% Prior LER
- 7% Prior limb amputation

Risk of MACE plus MALE 23.6%
at 3 years in fragile, 34% higher
comparing fragile vs not fragile

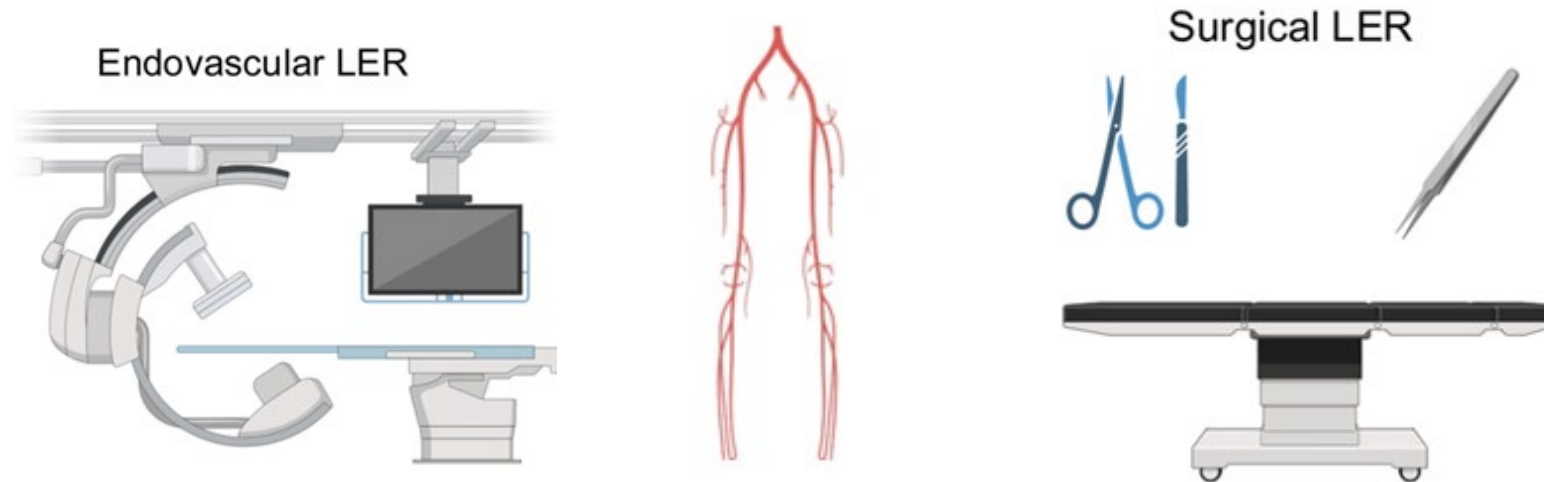


Rivaroxaban
+ low-dose aspirin
VS
Placebo
+ low-dose aspirin

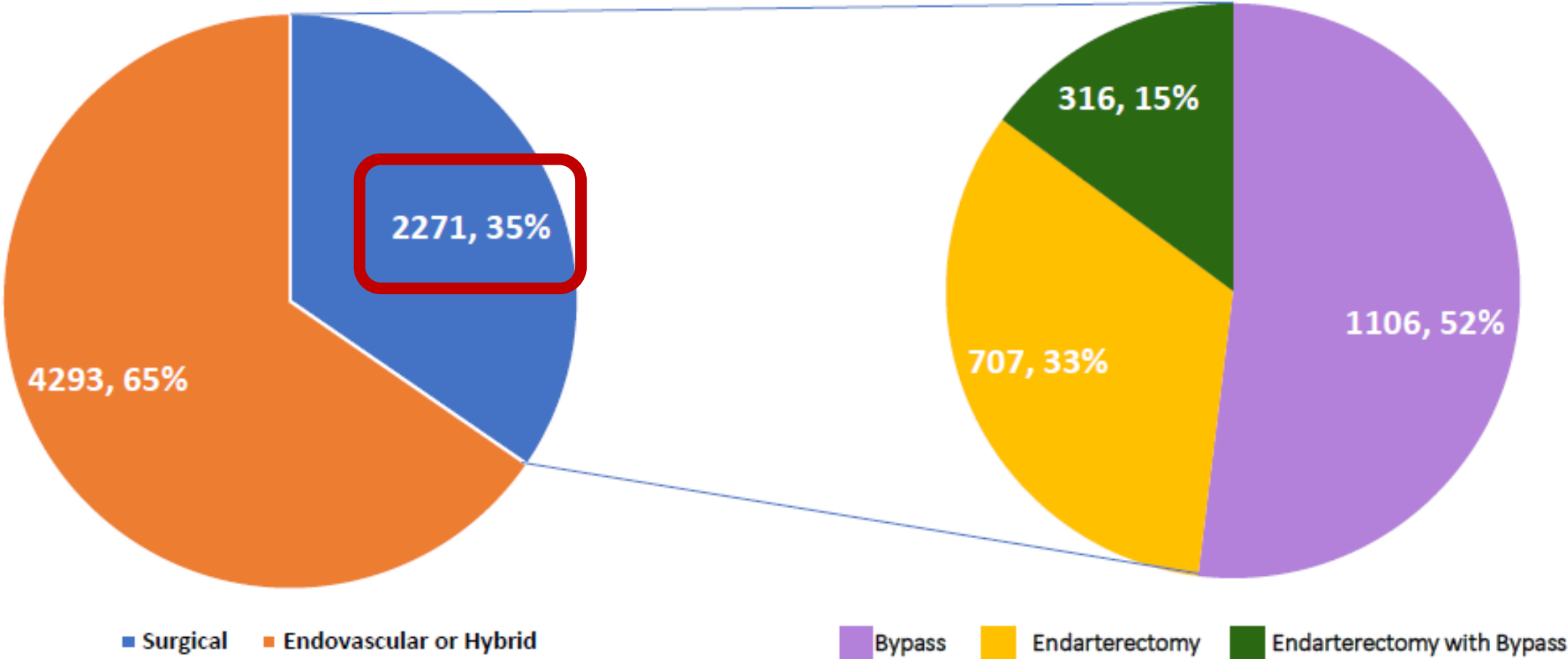
Cumulative Incidence of MALE



Efficacia della DPI in base al tipo di procedura di Rivascolarizzazione: Chirurgica vs Endovascolare?



Distribution of Surgical Revascularizations



	Surgical N = 2271	Endovascular N = 4293	P-value
Diabetes Mellitus	709 (31.2)	1920 (44.7)	<0.001

ALI in Subgroup with Diabetes:

a combined analysis insights VOYAGER PAD and ... Trial



Risk of bias legend

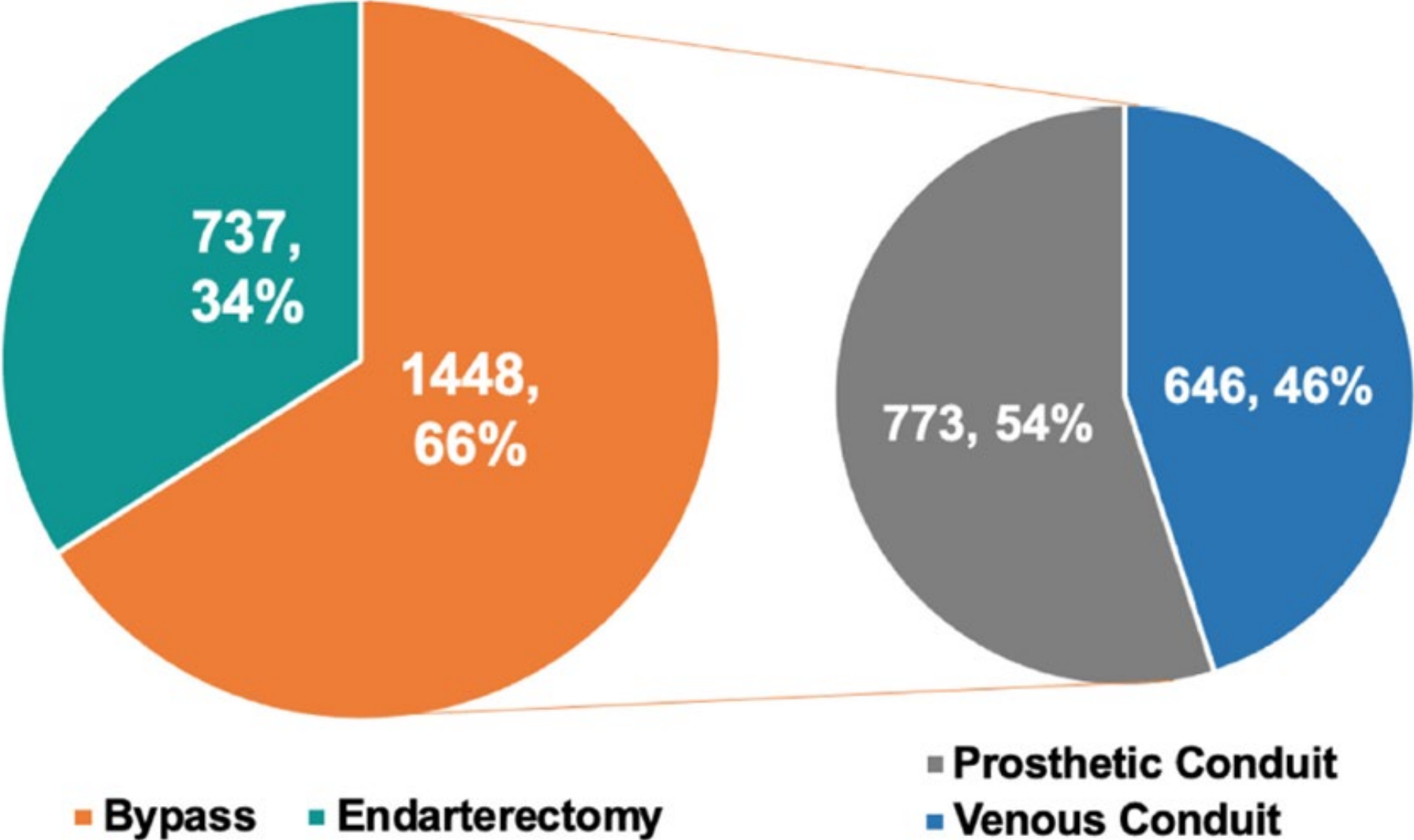
- (A) Random sequence generation
- (B) Allocation concealment
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Data are preliminary, unpublished, and should not be photographed, reproduced, distributed, or cited.



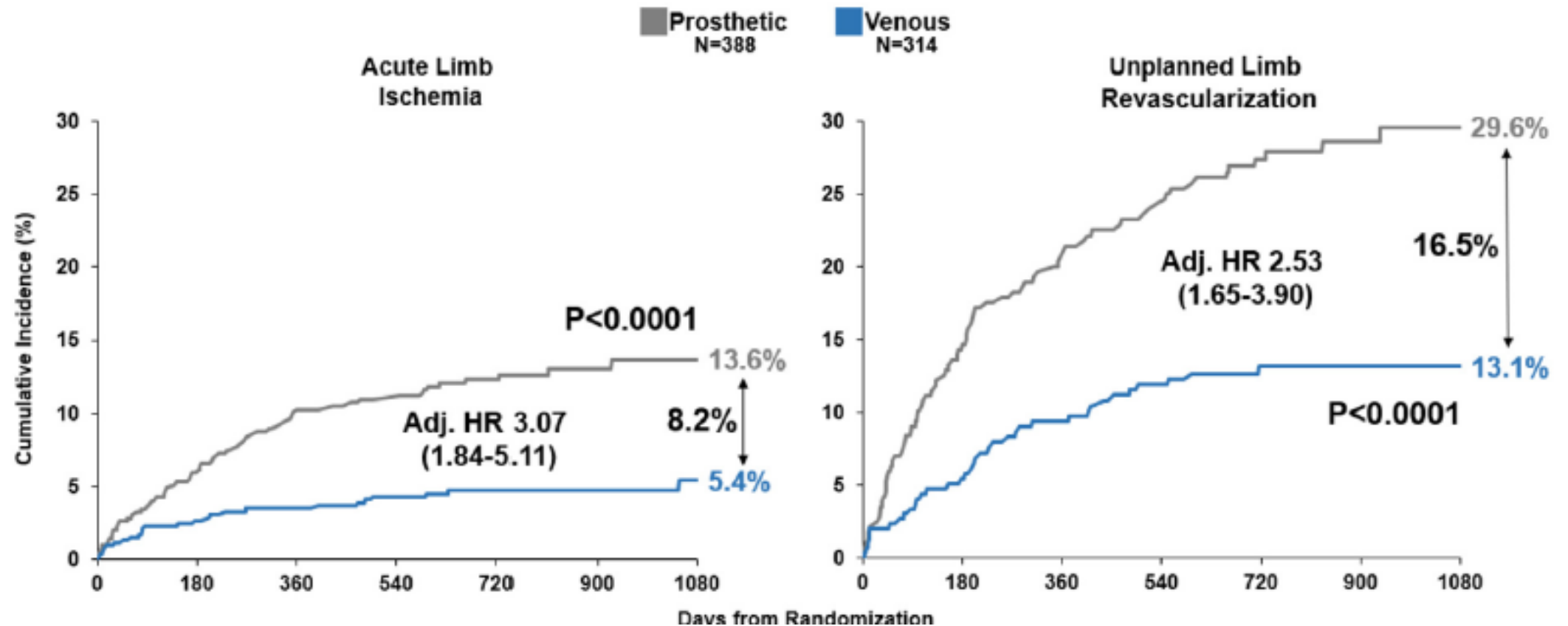
for updates

From
Riva
disea
pros
Govsy



	Venous N = 646	Prosthetic N = 773	P-value
Diabetes Mellitus	212 (32.8)	257 (33.2)	0.051

Higher incidence for unplanned limb revascularization and ALI at 3 years for prosthetic vs venous conduit bypass in placebo group



Adjust. for age, sex, history of hypertension, smoking status, history of diabetes, baseline eGFR <60 mL/min/1.73 m², history of peripheral revascularization, history of CLI, amputation, and distal bypass target artery

DPI efficacy on ALI at 3 years in prosthetic vs venous conduit bypass

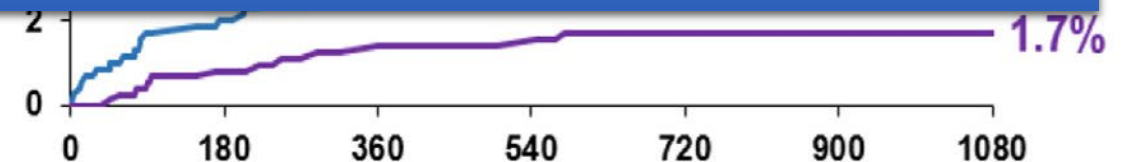
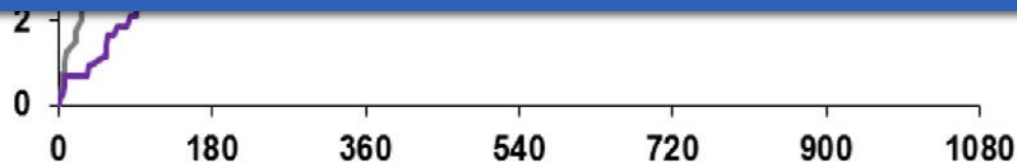
Prosthetic

P-interaction = 0.169

Acute Limb Ischemia

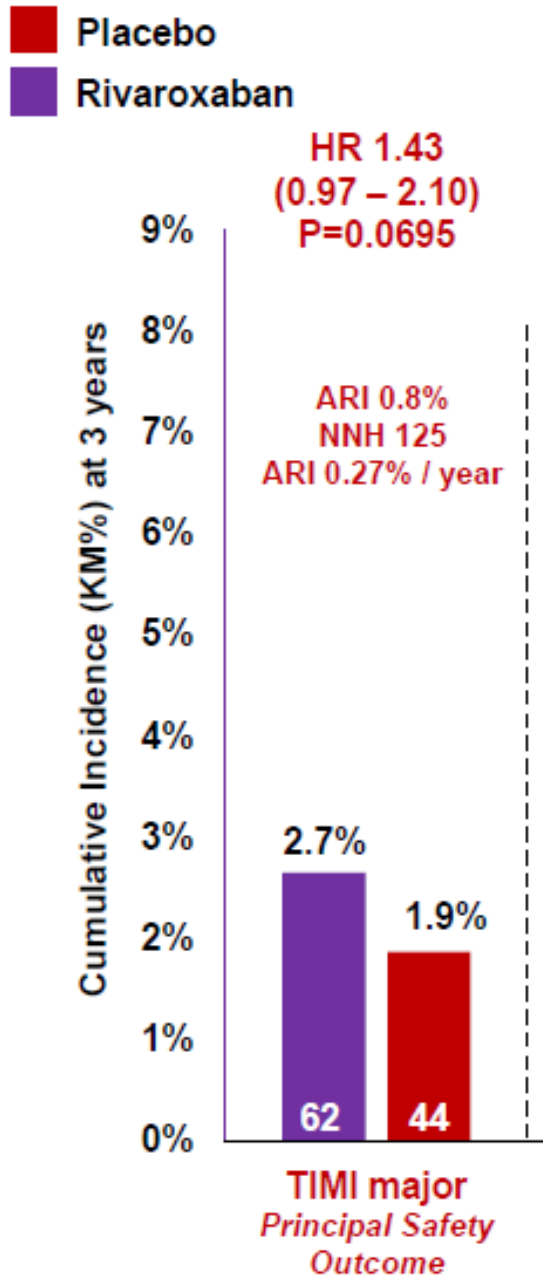
No evidence was found of a 3-way interaction between the study drug, conduit type and clopidogrel use ($p_{\text{interaction}} = 0.846$) for the primary composite outcome

Cumulative Incidence (%)



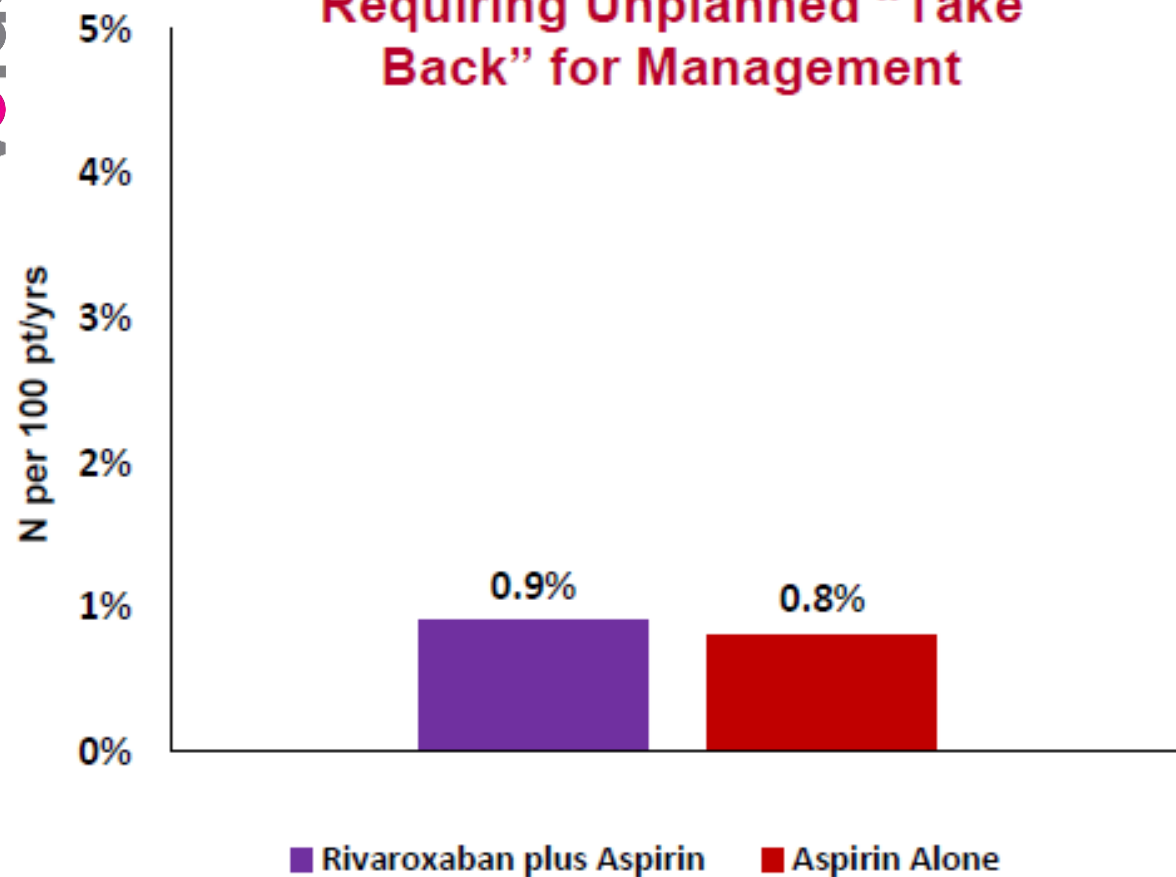
Days from Randomization

Safety

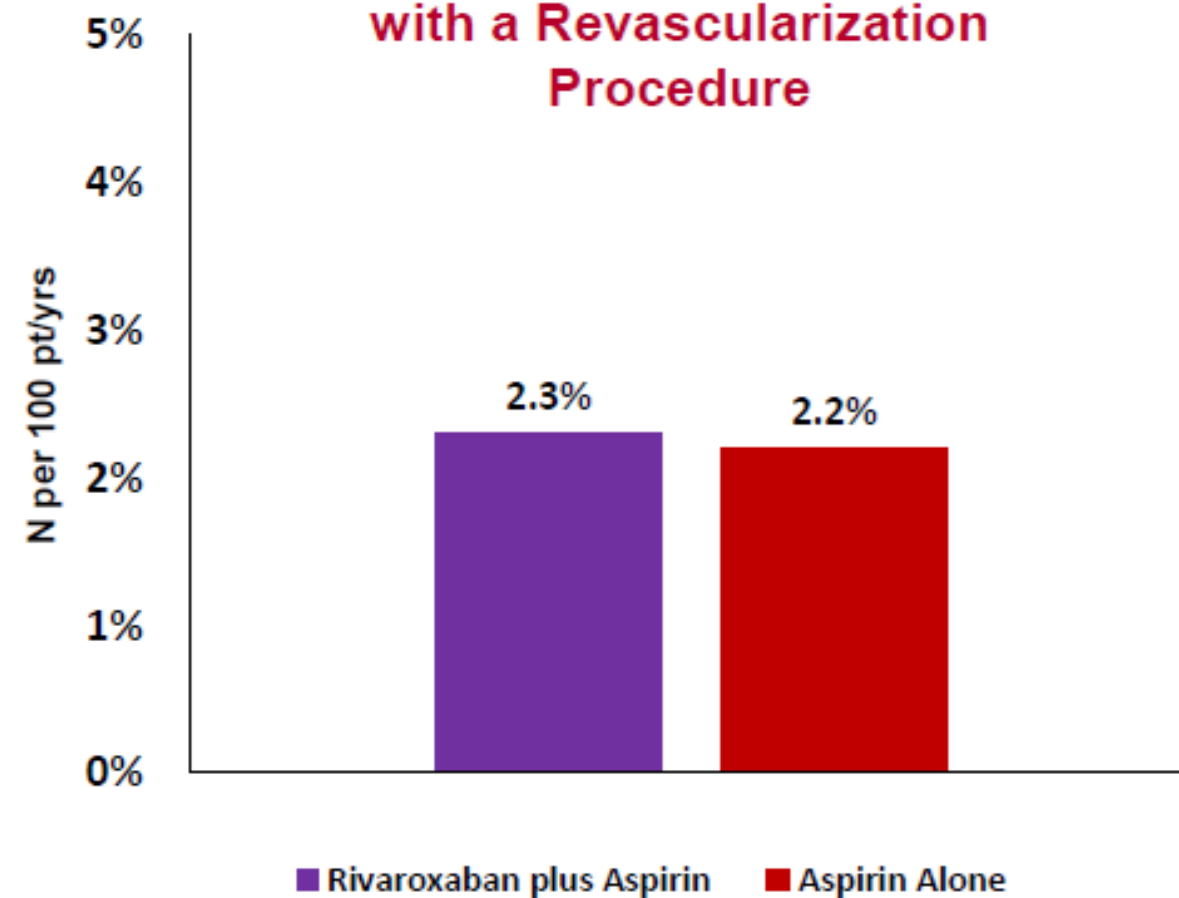


Procedural Bleeding

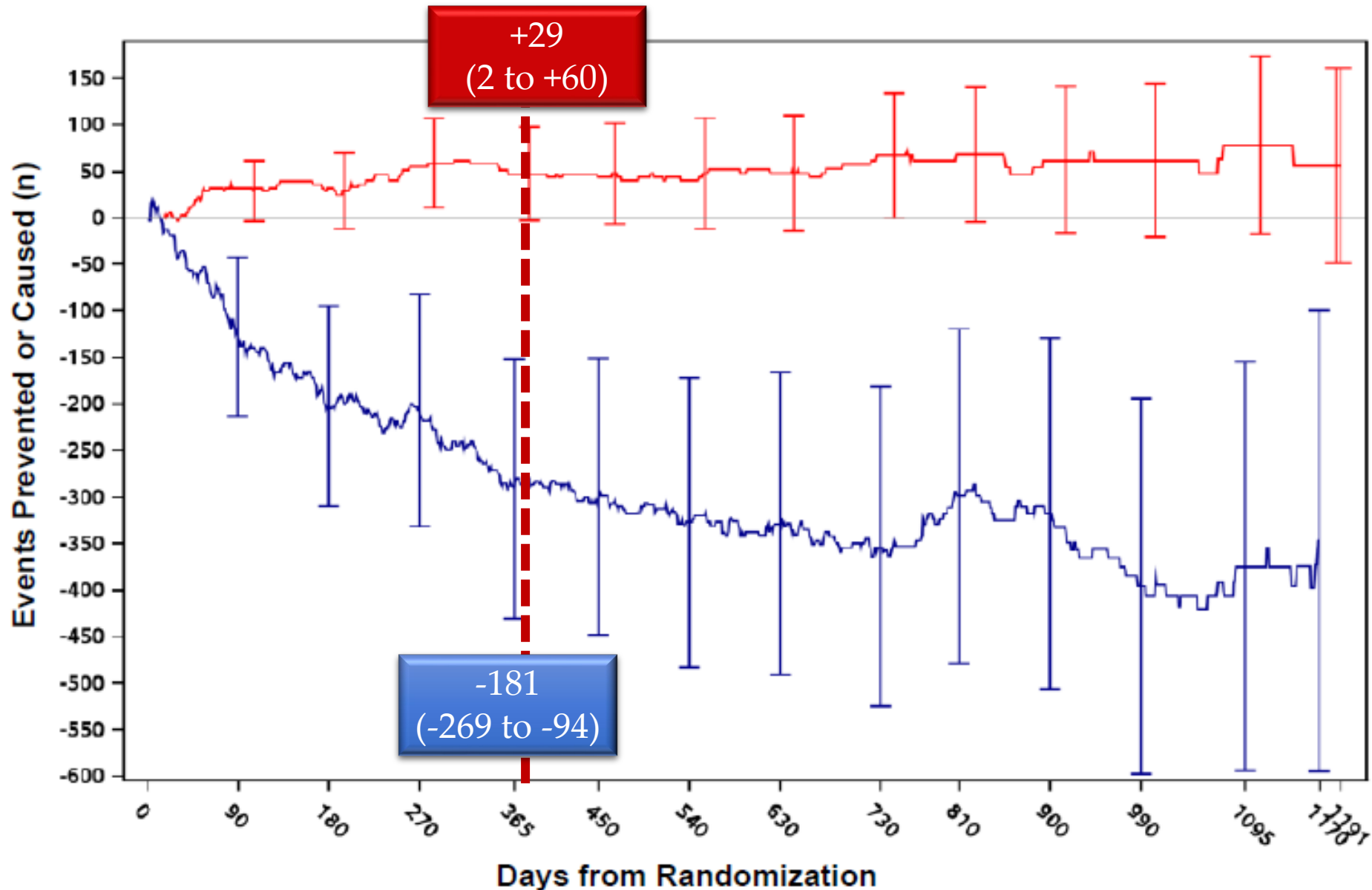
Post-Procedural Bleeding Requiring Unplanned “Take Back” for Management



Any Bleeding Associated with a Revascularization Procedure



Risk & Benefit Over Time



**TIMI major
bleeding**

Benefit-Risk Ratio
 $\approx 6:1$

**Primary endpoint
composite of acute limb
ischemia, major
amputation of vascular
cause, MI, ischemic
stroke or CV death**

Evidence supporting DPI in diabetic foot with critical ischemia derives mainly from the CLTI subgroup of VOYAGER-PAD, not from a DF dedicated trial



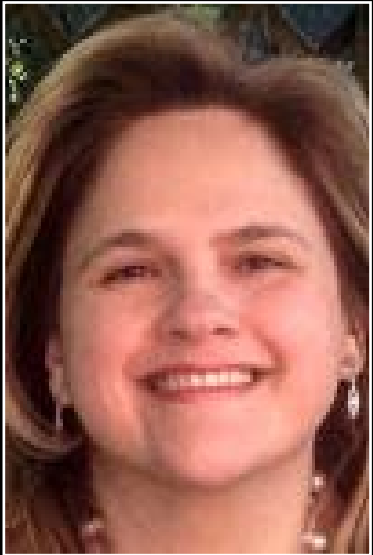
EVIDENCE GAP

- ✓ Ischemic ulcer included;
- X Major tissue loss excluded;
- ? WIfI stage;
- ? Diabetic foot ulcer prevalence

VOYAGER-PAD: WAS THE DIABETIC FOOT PATIENT REALLY REPRESENTED?

SAVE FOOT *for* SAVE LIFE

The Italian Kick-Off



Cristiana Vermigli



Stefano Radicchia



32 DF Centers
47 Specialists

704 Surveys





Study Aim

- ✓ *To design a web-based questionnaire on physicians use of dual-pathway inhibition (DPI) in diabetic patients diagnosed with ischemic diabetic foot syndrome in a real-word setting*





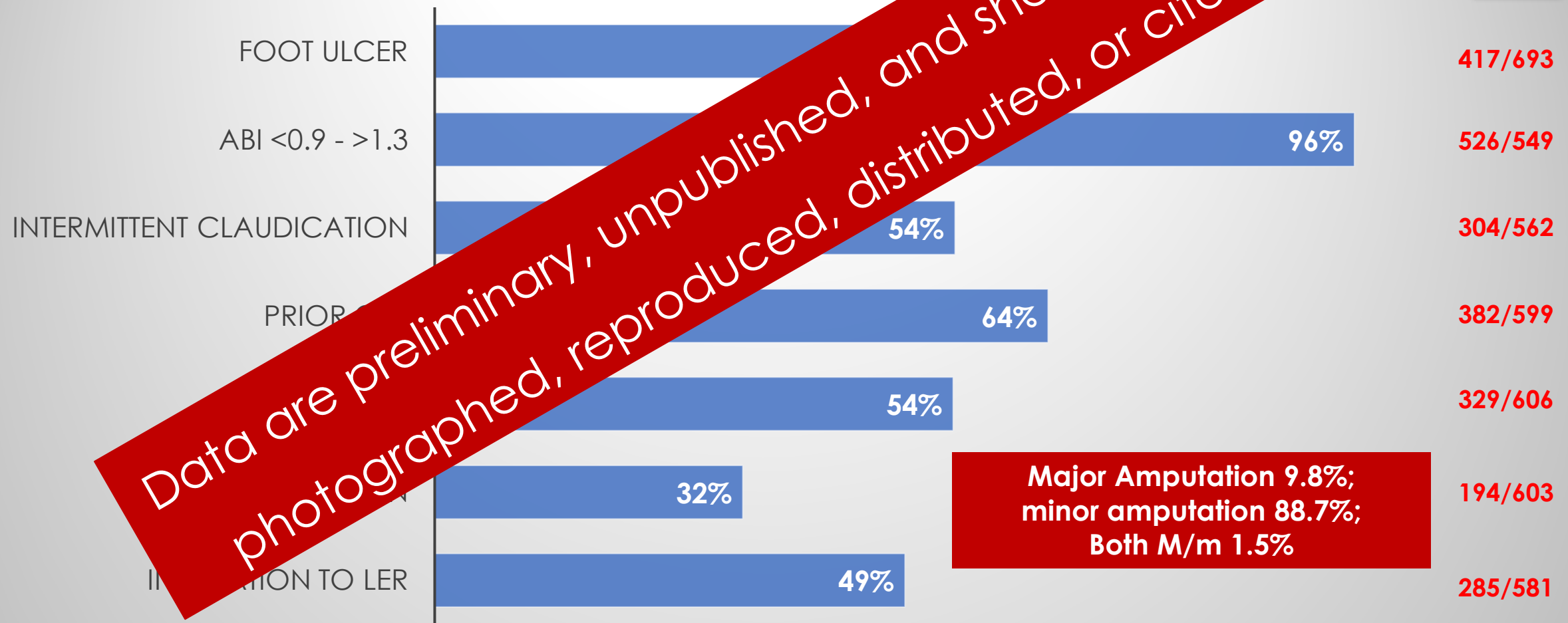
Clinical Characteristics

LEAD spectrum ("high-risk limb presen



693

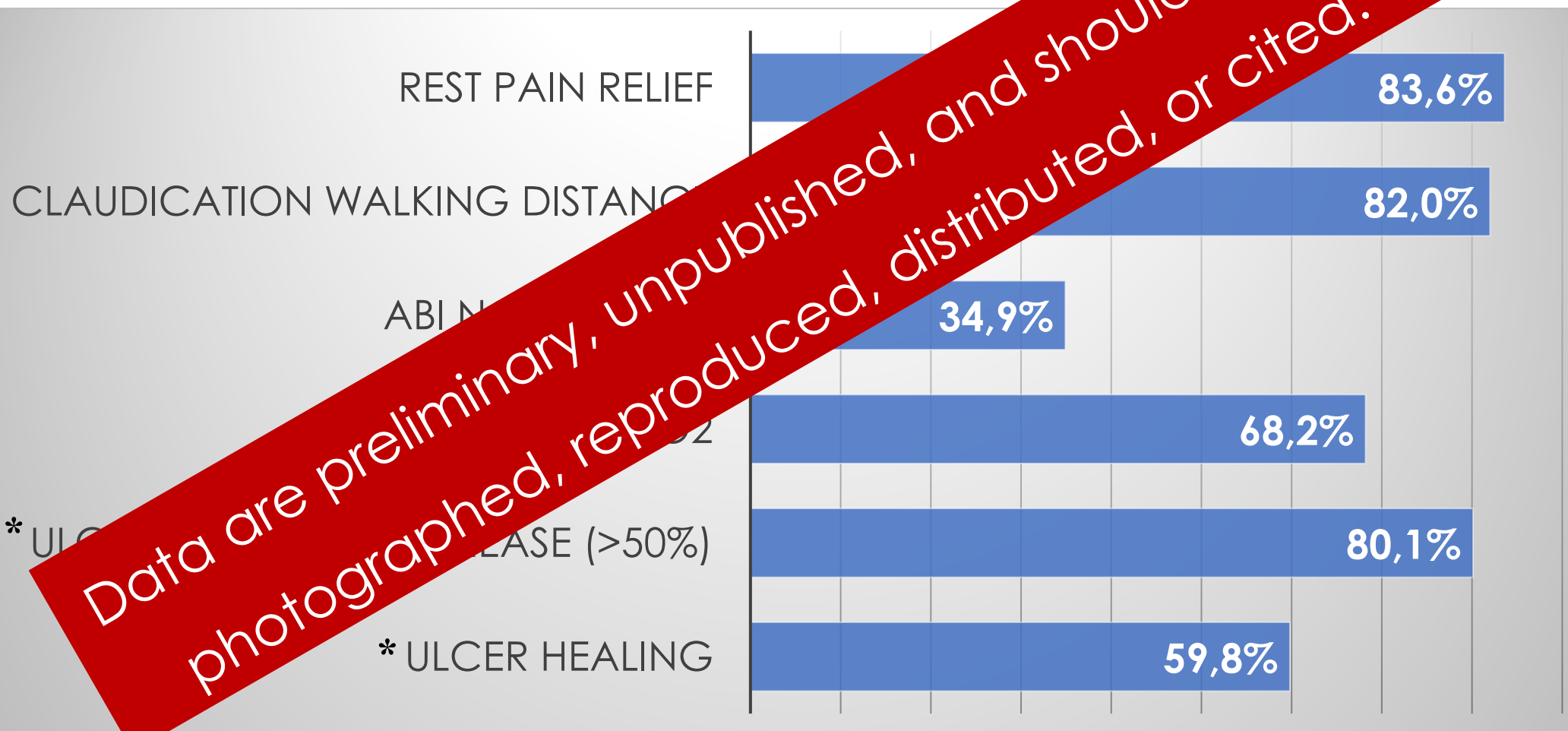
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Clinical Outcomes following a 12-month period after the initiation of DPI the

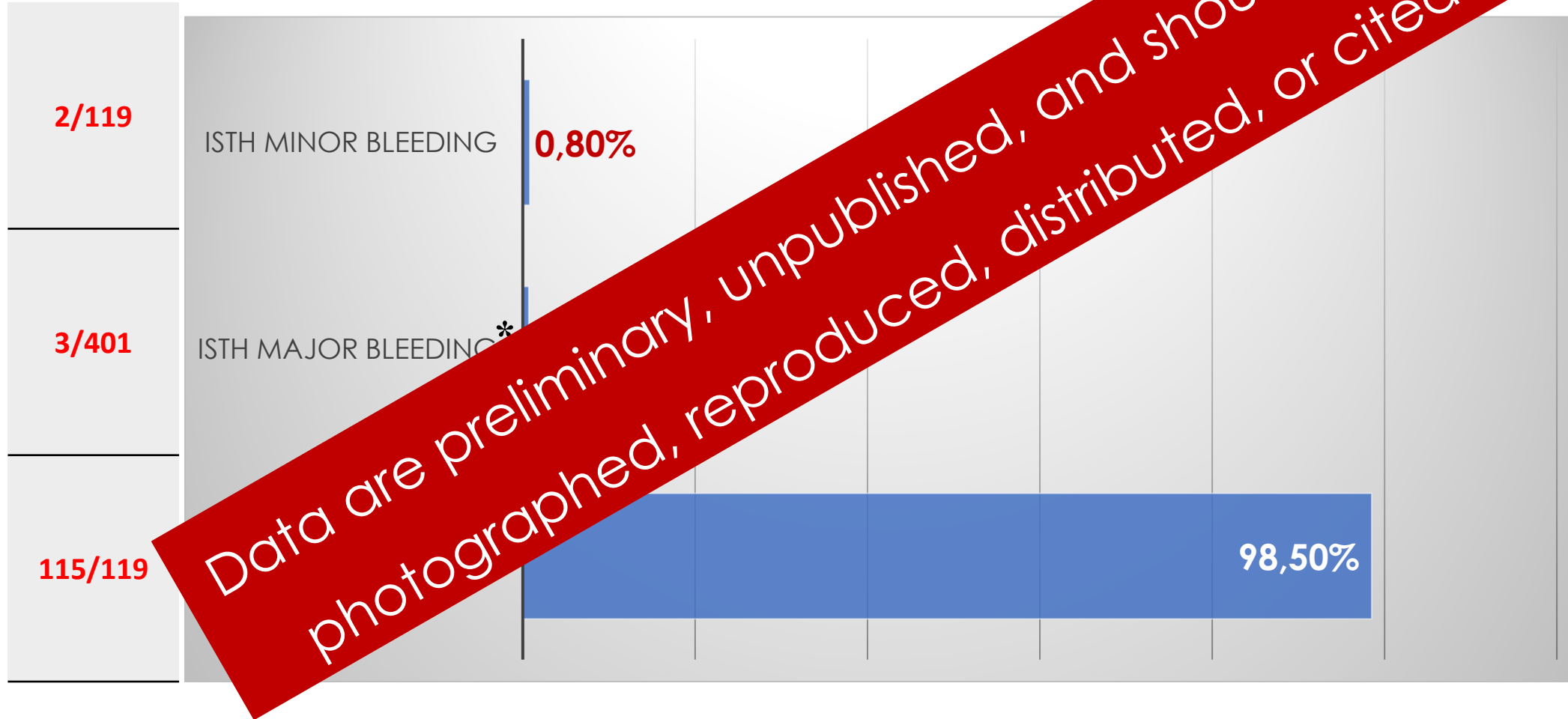


* Foot Ulcer Occurrence in the whole study cohort : 417/693 (60%); FU treated with standard of care



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Safety Outcomes: Bleeding



* ICH (1/403)

Clinical Akrasia (ἀκρασία):

evidence overruled by habit





*“Considerate la vostra semenza: fatti non
foste viver come bruti, ma per seguir
virtute e canoscenza”*

Major Bleeding definitions in Cardiovascular trials:

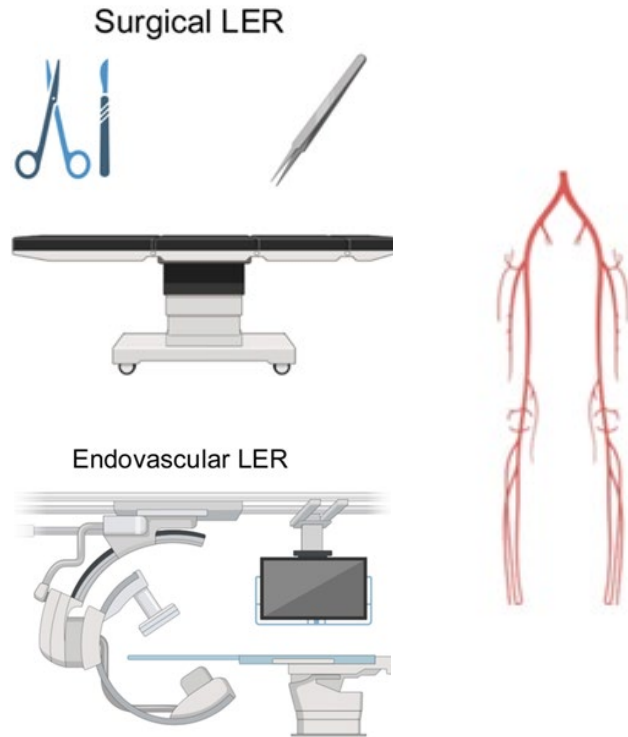
comparisons of TIMI, ISTH and BARC classifications

Major bleeding	TIMI	ISTH	BARC
Emorragia intracranica (ICH)	✓	✓	✓ (3c/5)
Hb drop	≥5 g/dL	≥2 g/dL	3a: 3-5 g/dL 3b: ≥5 g/dL
Trasfusione ≥2 U	No (non criterio autonomo)	✓	Inclusa nel tipo 3
Fatal bleeding	✓	✓	✓ tipo 5
Organo critico	Limitato a ICH	✓ definizione esplicita	✓ class. dettagliata

TIMI: Rao AK et al. Circulation. 1988; ISTH: Schulman S, Kearon C. J Thromb Haemost. 2005; BARC: Mehran R et al. Circulation. 2011.

DPI in Pts With PAD Undergoing LER With and Without History of Prior Limb Revascularization

2336/6564 (35.5%) pts



Baseline Characteristics - Prior LER

Median age 67 years

25% Female

86% Hypertension

42% Diabetes mellitus

71% Hyperlipidemia

13% Prior MI

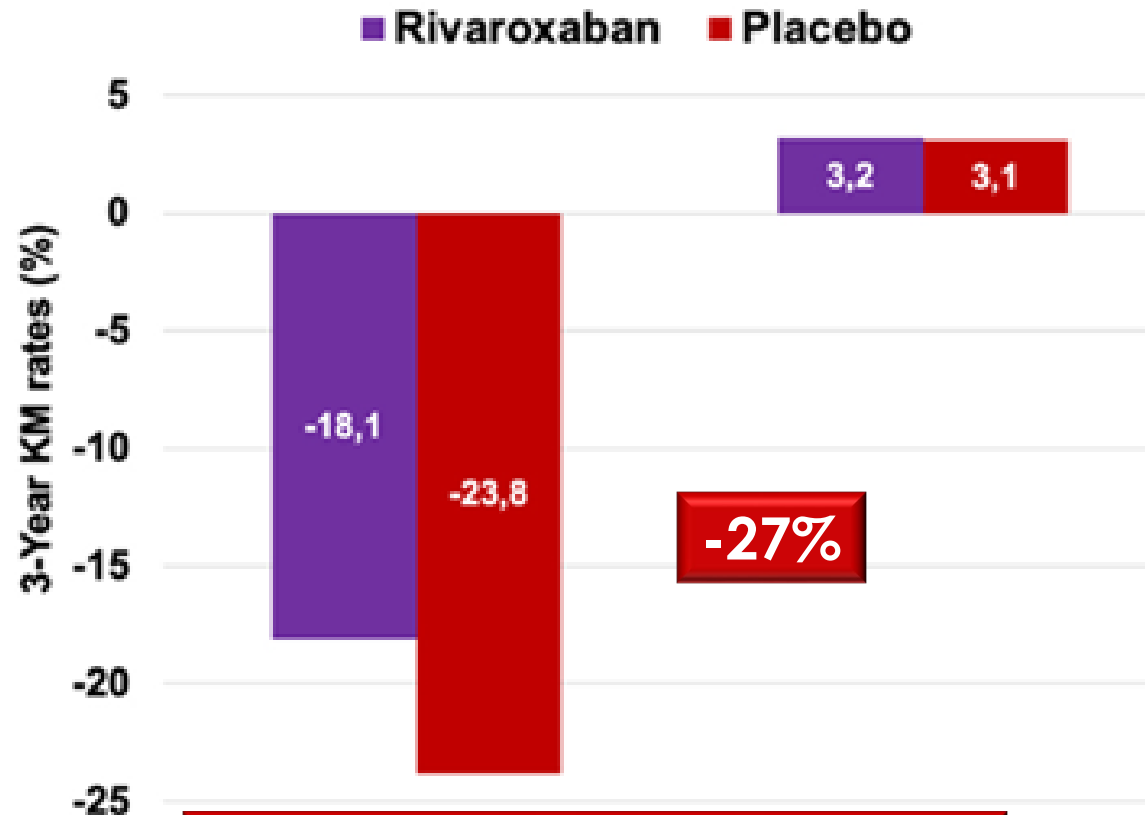
18% CLTI

7% Prior amputation

Prior LER

MACE and MALE
HR 0.73 (0.60-0.88)

TIMI Major Bleeding
HR 1.08 (0.62-1.89)



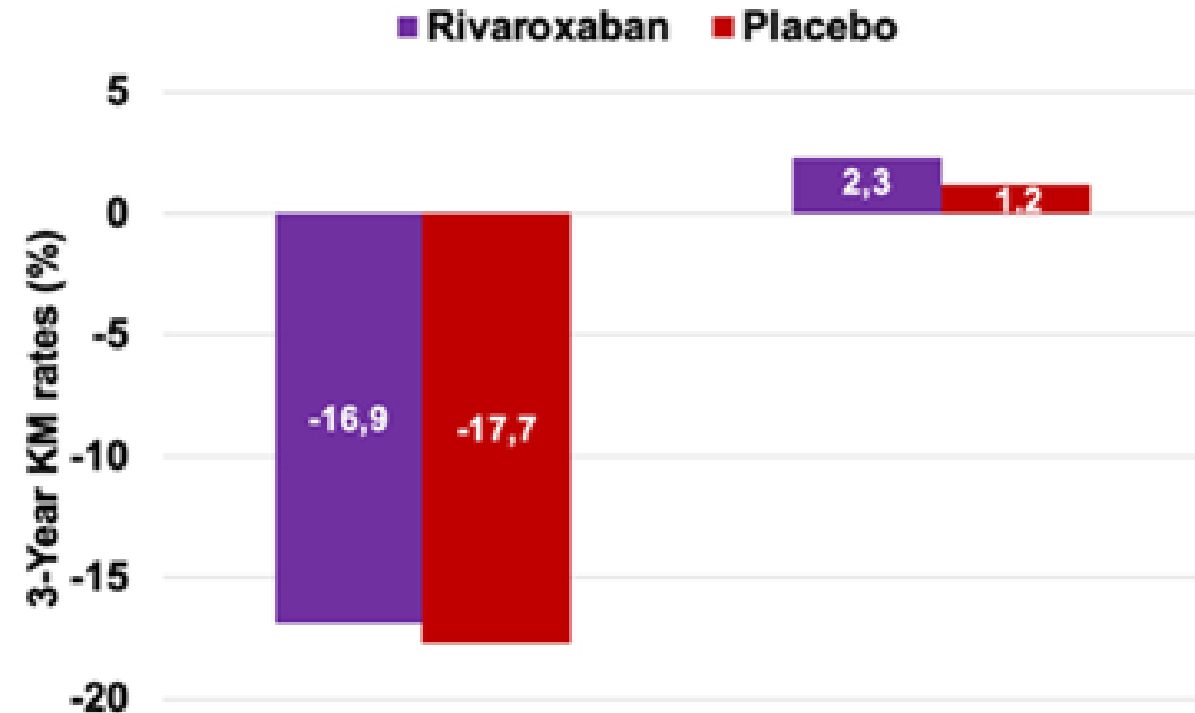
HR 0.73 (95%CI 0.60-0.88)
ARR 5.7% [95% CI 2.0-9.4]

HR P_{int} = 0.036

No Prior LER

MACE and MALE
HR 0.94 (0.81-1.10)

TIMI Major Bleeding
1.88 (1.09-3.25)



HR 0.94 (95%CI 0.81-1.10)
ARR 0.8% [95% CI -1.9 to 3.5]

Lack of efficacy for anti-thrombotic strategies on MALE and MACE risk reduction after peripheral intervention for CLI:

The CASPAR and The Dutch Bypass Oral Anticoagulants or Aspirin (BOA) Trials

