Incident Hypertension in REPRIEVE: Risk Factors, Pitavastatin Effect & Cardiovascular Consequences

Esteban Martínez[1], MD, PhD, Maya Watanabe[2], MS, Risa Hoffman[3], MD, Markella V. Zanni[4], MD, Anton Pozniak[5], MD, Saate S. Shakil[6], MD, Sara McCallum[4], MPH, Sarah M. Chu[4], MSN, Suman Srinivasa[4], MD, Carlos D. Malvestutto[7], MD, Carl J. Fichtenbaum[8], MD, Gerald S. Bloomfield[9], MD, Craig A. Spons eller[10], MD, Alex B. Lu[4], BAS, Michael T. Lu[11], MD, Judith A. Aberg[12], MD, Judith S. Currier[3], MD, Pame la S. Douglas[13], MD, Heather J. Ribaudo[2], PhD, Steven K. Grinspoon[4], MD

[1]Department of Infectious Diseases, Hospital Clínic, IDIBAPS, University of Barcelona, Barcelona, Spain; CIBER de Enfermedades Infecciosas, Instituto de Salud Carlos III, Madrid, Spain; Rei al Acadèmia de Medicina de Catalunya, Barcelona, Spain. [2]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, United States of America.[3]Division o f Infectious Diseases, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA.[4]Metabolism Unit, Massachusetts General Hospital and Harvard Medical S chool, Boston, MA, USA.[5]Chelsea and Westminster Hospital and London School of Hygiene and Tropical Medicine, London, UK.[6]Department of Medicine, University of California, Los Angeles , Los Angeles, CA, USA.[7]Division of Infectious Diseases, Ohio State University Medical Center, Columbus, United States of America.[8]Division of Infectious Diseases, Department of Medicine, University of Cincinnati, Cincinnati, OH, USA.[9]Department of Medicine, Duke Global Health Institute and Duke Clinical Research Institute, Duke University, Durham, NC, USA.[10]Kowa Pharmac euticals America, Inc., Montgomery, AL, USA. [11]Cardiovascular Imaging Research Center, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. [12]Division of Infecti ous Diseases, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [13]Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA.

National Heart, Lung, and Blood Institute

National Institute of Allergy and Infectious Diseases

ACTG

Kowa

GILEAD

ViiV Healthcare

neatid

MGH 1811

CROI 2026

Background and Objectives

- PLWH have elevated cardiovascular risk despite virologic control.[1]
- Hypertension is common and strongly contributes to ASCVD risk.[2,3]
- The effect of statins on incident hypertension in PLWH is unknown.

Objective:

- To determine the **effect of pitavastatin on incident hypertension** and evaluate its association with subsequent MACE in REPRIEVE
- To evaluate **risk factors of incident hypertension**

1. So-Armah K et al. *Lancet HIV* 2020; 4. Bigna JJ et al. *BMC Med* 2021; 6. Hoffman RM et al. *CROI* 2026 (Abstract 676)

Methods

- Secondary analysis of the **REPRIEVE trial**
  - **Randomized** pitavastatin 4 mg vs placebo
- Included participants **without hypertension at REPRIEVE entry** (N=4989)
  - Hoffman *CROI* 2026 (Abstract 676)

Outcomes:

- **Incident hypertension**
  Time from randomization to hypertension diagnosis (death as competing event)
  - Targeted clinical diagnosis in REPRIEVE
  - Guided by standard BP criteria
    - SBP ≥140 or DBP ≥90 mmHg
- **Major Adverse Cardiovascular Events (MACE)**

Statistical analysis:

- Effect of pitavastatin on incident hypertension:
  → Cause-specific Cox models
- Risk factors for incident hypertension
  → Poisson regression
- Association between hypertension and MACE:
  → Fine–Gray models
  → Hypertension as time-updated exposure
  → Stratified by treatment arm

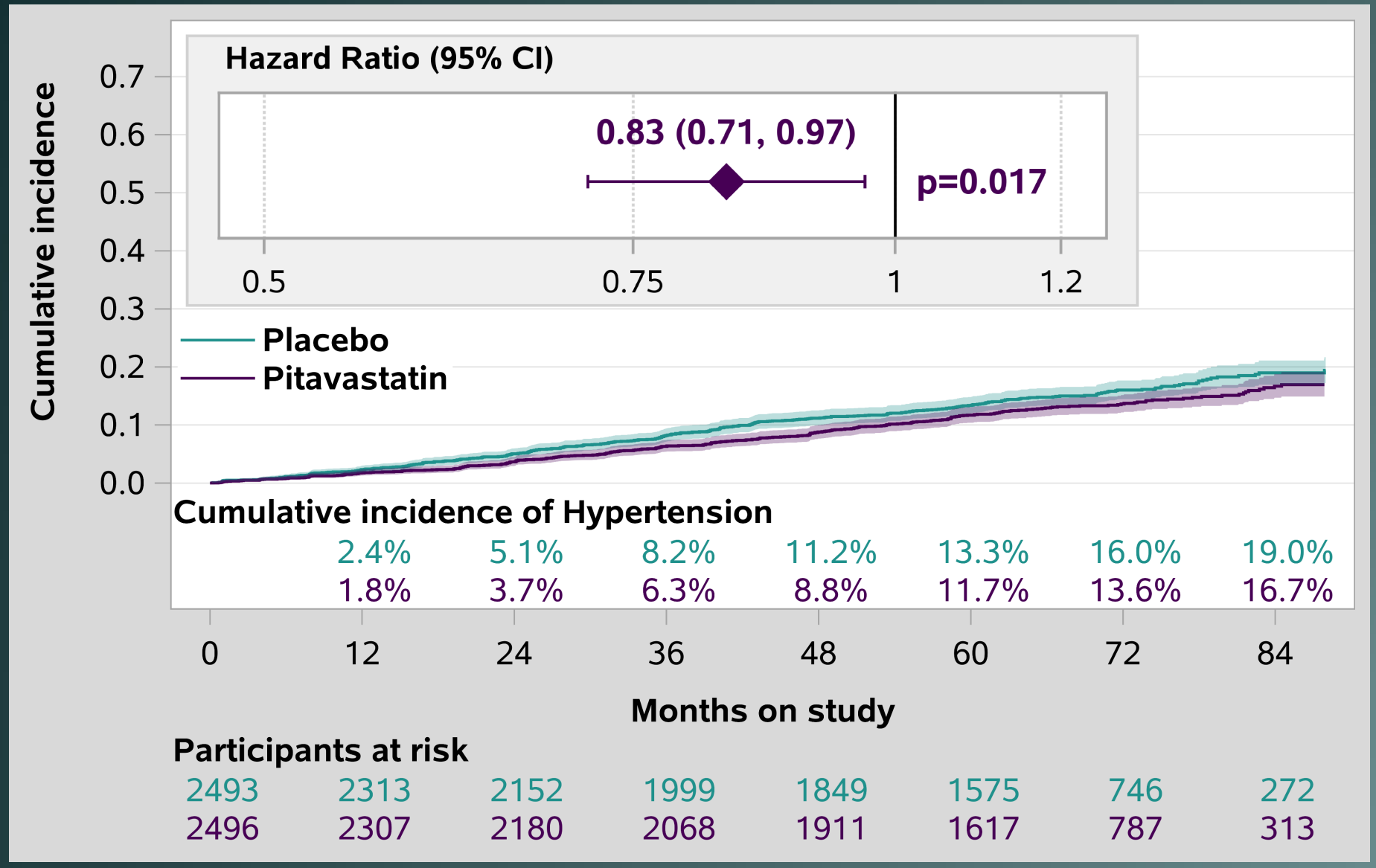
Participant characteristics (N=4989)

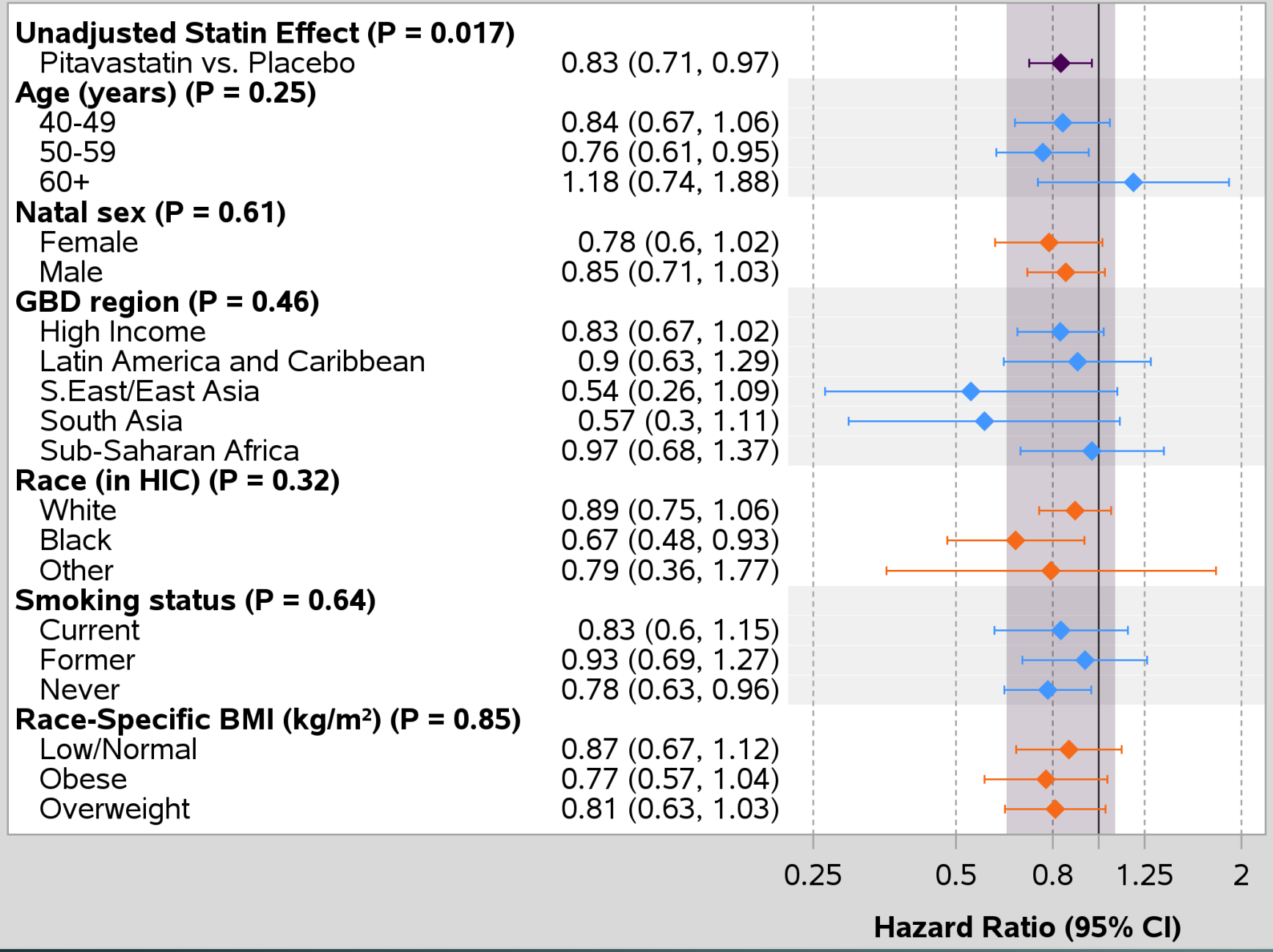
	Pitavastatin (n=2496)	Placebo (n=2493)
Age, years	**49 (45–54)**	**49 (45–54)**
Female sex	**30%**	**29%**
Global region		
• High income	**51%**	**51%**
• Latin America/Caribbean	**18%**	**18%**
• Sub-Saharan Africa	**15%**	**15%**
Race (within HIC)		
• White	**58%**	**57%**
• Black	**36%**	**37%**
• Other	**6%**	**6%**
Obese BMI	**18%**	**17%**
eGFR <90 mL/min/1.73m²	**41%**	**41%**
ASCVD risk score	**3.5 (1.6–6.1)**	**3.7 (1.6–6.2)**
Systolic BP (mmHg)	**119 (110–127)**	**120 (110–126)**
Diastolic BP (mmHg)	**76 (70–80)**	**76 (70–80)**

	Pitavastatin (n=2496)	Placebo (n=2493)
Met. Syn. components		
• Elevated BP	**23%**	**24%**
• Reduced HDL-C	**35%**	**36%**
• Elevated triglycerides	**31%**	**30%**
• Elevated waist circumference	**43%**	**42%**
• Elevated fasting glucose	**15%**	**16%**
Sodium intake		
• Optimal	**24%**	**23%**
• Suboptimal/Poor	**76%**	**77%**
CD4 cells/mm³	**615 (447–827)**	**623 (445–814)**
HIV RNA <LLQ	**87%**	**88%**
ART regimen		
• NRTI + NNRTI	**49%**	**48%**
• NRTI + INSTI	**24%**	**24%**
• NRTI + PI	**19%**	**19%**
ART duration, y	**9.2 (5.2–14.2)**	**9.1 (5.0–14.3)**

Statistics for continuous variables are Median (Q1-Q3)

Cumulative Incidence of Hypertension by Treatment



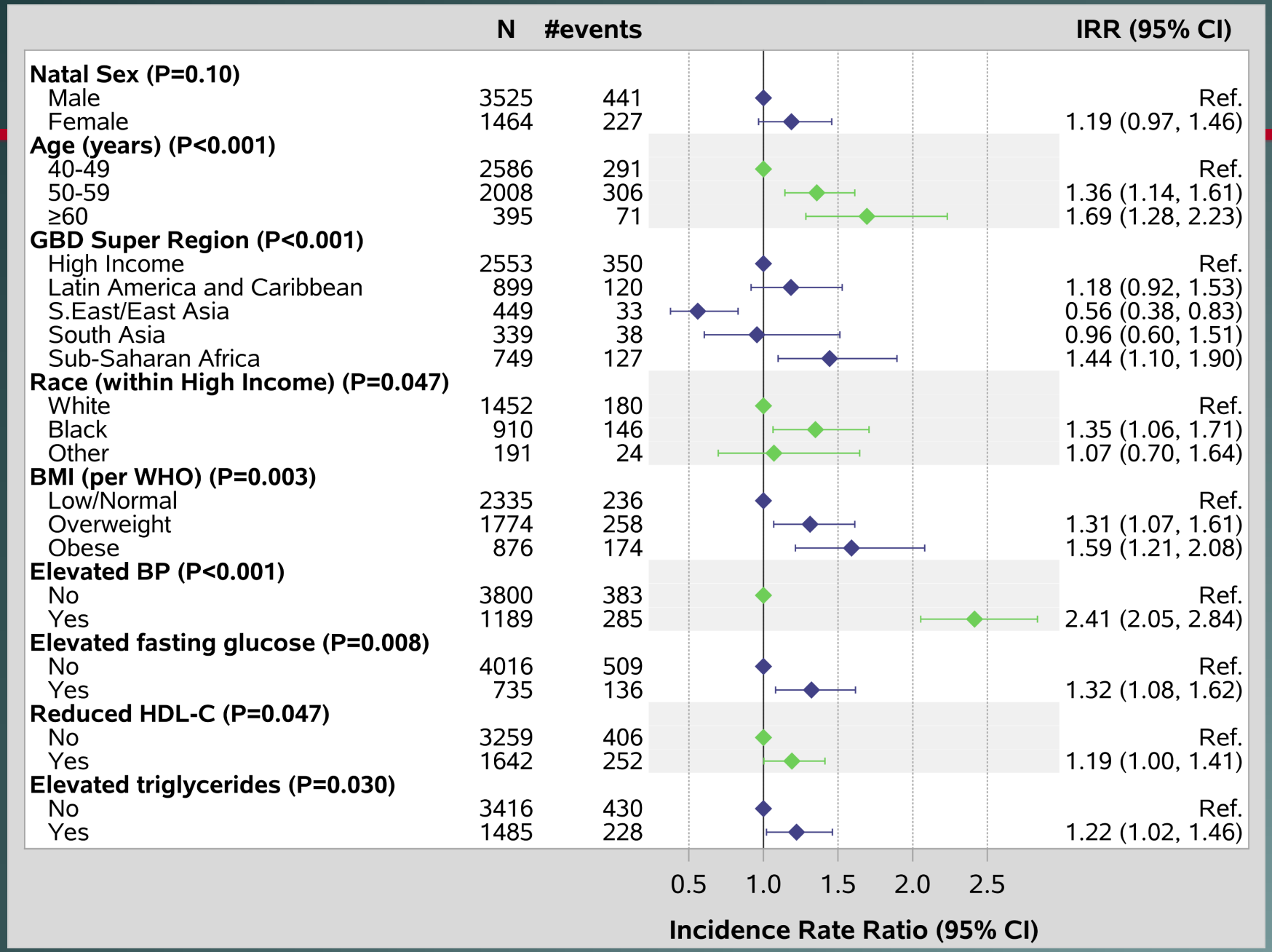


Consistent Statin Effect Across Subgroups

Some variability with older age by region

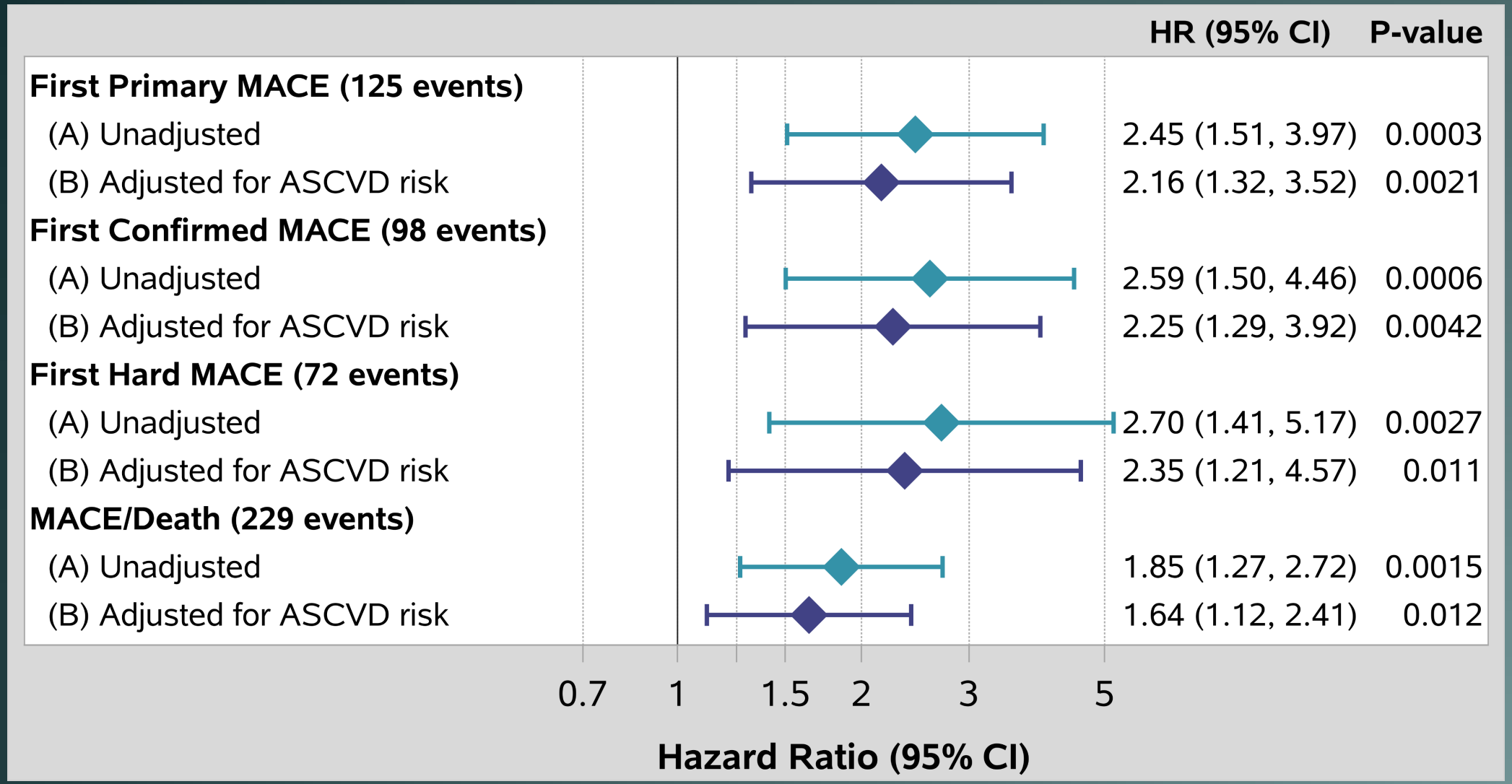
Risk factors of incident hypertension

Adjusted analysis



Model also adjusts for cigarette smoking (P=0.70), eGFR (P=0.58), elevated waist circumference (P=0.75), CD4 cell count (P=0.23), and randomized treatment (P=0.034)

Time-updated Hypertension and MACE



Strengths & Limitations

Strengths

- Large, global RCT population
- Participants free of HTN at baseline
- Randomized, double-blind intervention
- Prespecified targeted diagnosis
- Adjudicated MACE outcomes

Limitations

- Incident HTN based on site-reported diagnosis
- Limited power for some subgroup analyses
- No detailed data on lifestyle interventions
- BP was only captured in the database at annu al visits
- Secondary analysis

Conclusions and Future Directions

- In PLWH at low-to-moderate ASCVD risk, **pitavastatin reduced incident hypertension**.

- Incident hypertension was **associated with a substantially higher risk of subsequent MACE during follow-up**, independent of baseline ASCVD risk.

- These findings suggest that **statin benefits in HIV may extend beyond lipid lowering**.

- Results support **integrated cardiovascular prevention in HIV care**, including proactive blood pressure screening and management.

- Further research should clarify mechanisms linking statins, hypertension, and vascular risk, and optimize combined lipid and blood pressure strategies.

Acknowledgements

- REPRIEVE Participants
- Site teams and Investigators
- Funders:
  - NIH
  - Kowa Pharmaceuticals America
  - Gilead Sciences
  - ViiV Heathcare
  - Instituto de Salud Carlos III
  - European Regional Development Fund