SOLOIST SCORED

Benefits of SGLT1/2 Inhibition with Sotagliflozin Across Baseline Kidney Function

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on Behalf of the **SOLOIST-WHF** and **SCORED** Investigators

BWH

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Disclosures

Dr. Deepak L. Bhatt discloses the following relationships - Advisory Board: Boehringer Ingelheim, Cardax, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, Janssen, Level Ex, Medscape Cardiology, MyoKardia, NirvaMed, Novo Nordisk, PhaseBio, PLx Pharma, Regado Biosciences, Stasys; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: Inaugural Chair, American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Boston Scientific (Chair, PEITHO trial), Cleveland Clinic (including for the ExCEED trial, funded by Edwards), Contego Medical (Chair, PERFORMANCE 2), Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine (for the ENVISAGE trial, funded by Daiichi Sankyo), Novartis, Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Chair, ACC Accreditation Oversight Committee), Arnold and Porter law firm (work related to Sanofi/Bristol-Myers Squibb clopidogrel litigation), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim; AEGIS-II executive committee funded by CSL Behring), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Canadian Medical and Surgical Knowledge Translation Research Group (clinical trial steering committees), Cowen and Company, Duke Clinical Research Institute (clinical trial steering committees, including for the PRONOUNCE trial, funded by Ferring Pharmaceuticals), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), K2P (Co-Chair, interdisciplinary curriculum), Level Ex, Medtelligence/ReachMD (CME steering committees), MJH Life Sciences, Piper Sandler, Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); **Research Funding**: Abbott, Afimmune, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Cardax, CellProthera, Cereno Scientific, Chiesi, CSL Behring, Eisai, Ethicon, Faraday Pharmaceuticals, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Garmin, HLS Therapeutics, Idorsia, Ironwood, Ischemix, Janssen, Javelin, **Lexicon**, Lilly, Medtronic, MyoKardia, NirvaMed, Novartis, Novo Nordisk, Owkin, Pfizer, PhaseBio, PLx Pharma, Regeneron, Roche, **Sanofi**, Stasys, Synaptic, The Medicines Company, 89Bio; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Abbott, Biotronik, Boston Scientific, CSI, St. Jude Medical (now Abbott), Philips, Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Merck, Takeda.

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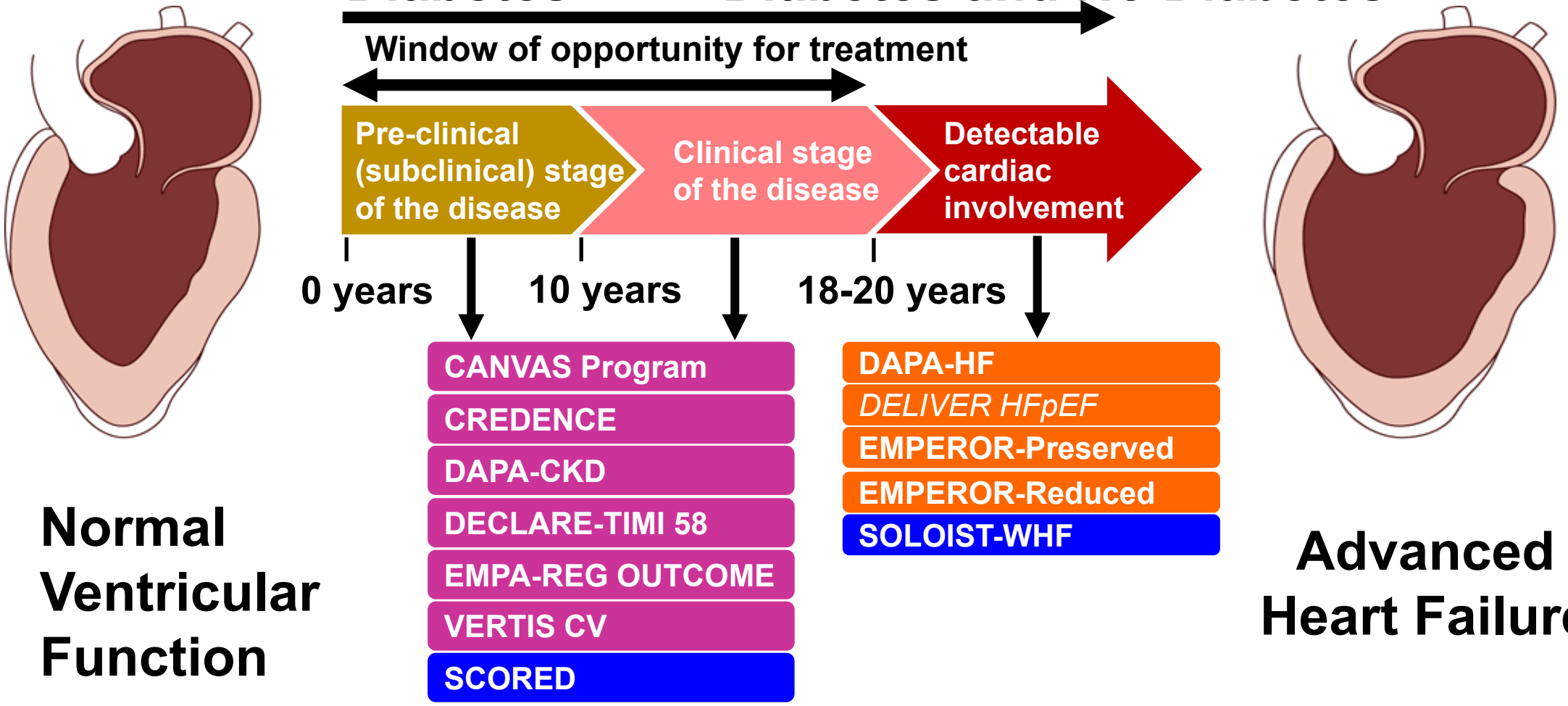
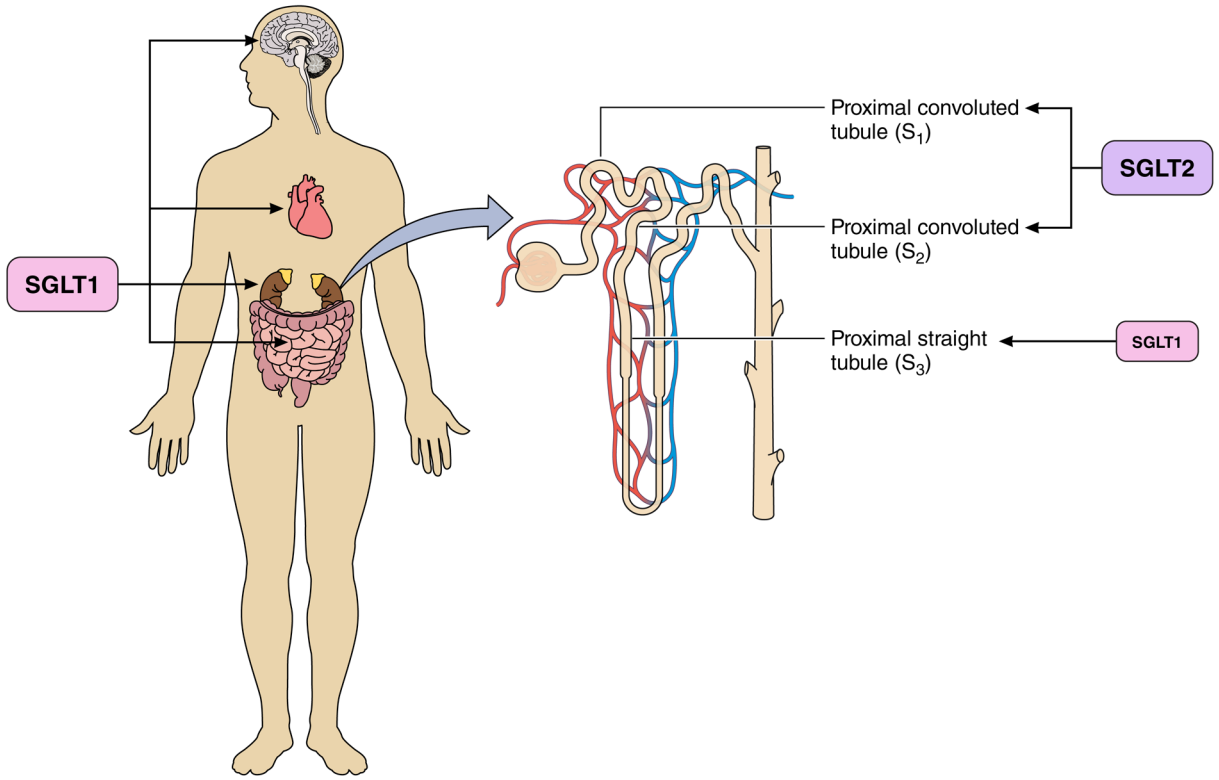
This presentation includes off-label and investigational uses of drugs.

The Evolution of SGLT2i in HF Management



Adapted from Bhatt DL, Verma S, Braunwald E. *Cell Metabolism*. 2019;30:847-849.

Sotagliflozin: Dual SGLT1 and SGLT2 Inhibitor

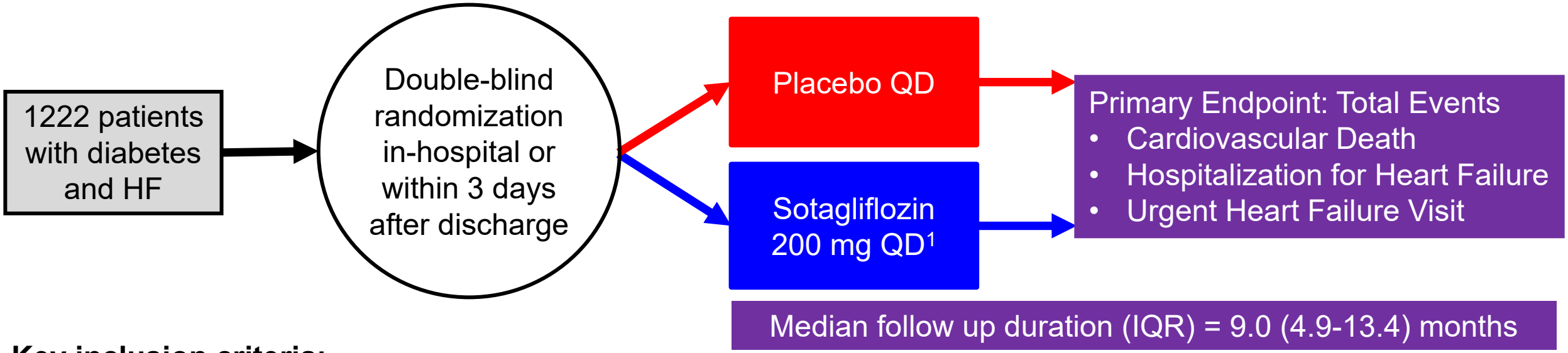


- **SGLT1** is the primary transporter for absorption of glucose and galactose in the GI tract
- Pharmacologic inhibition by sotagliflozin is independent of insulin and does not depend on kidney function
- Potential effects on atherosclerotic risks

- **SGLT2** is expressed in the kidney, where it reabsorbs 90% of filtered glucose
- Pharmacologic inhibition by sotagliflozin is independent of insulin but requires kidney function

Pitt B, Bhatt DL. *Circulation*. 2021.

SOLOIST-WHF Study Design



Key inclusion criteria:

- Admission with signs and symptoms of HF
- Treatment with intravenous diuretics
- Stabilized, off oxygen, transitioning to oral diuretics
- BNP ≥150 pg/mL (≥450 pg/mL if afib) or NT-proBNP ≥600 pg/mL (≥1800 pg/mL if afib)
- Type 2 diabetes

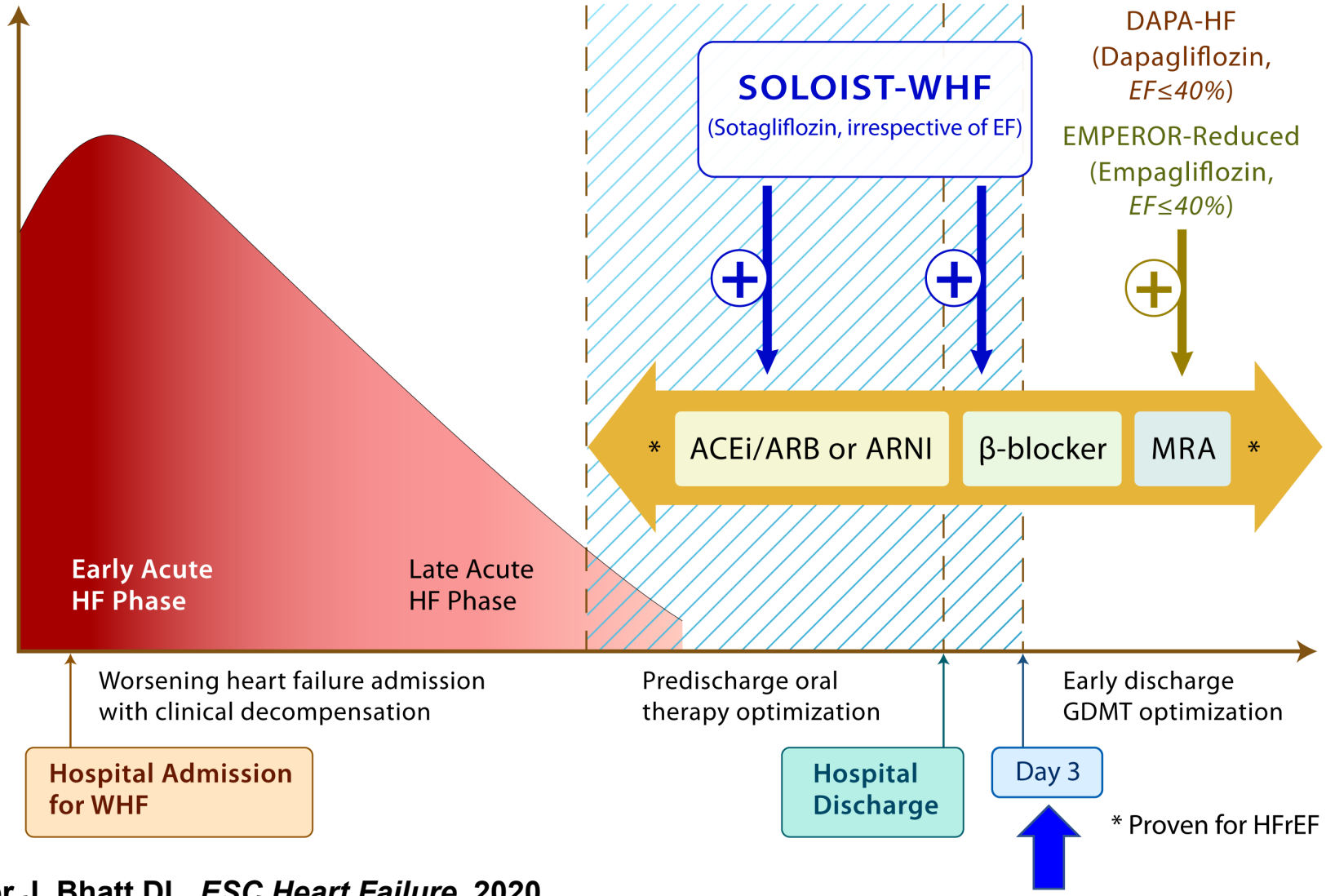
Key exclusion criteria:

- End-stage HF
- Recent ACS, stroke, PCI, or CABG
- eGFR <30 mL/min/1.73m^2

[1]Goal of dose increase to 400 mg QD
[2]HF or reasons other than HF

Bhatt DL, Szarek M, Steg PG, et al., and Pitt B. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.

SOLOIST-WHF: Addressing the Vulnerable Period of an Admission for Worsening Heart Failure



Verma S, Anker SD, Butler J, Bhatt DL. *ESC Heart Failure.* 2020.

Primary Efficacy: Total CV Death, HHF, and Urgent HF Visit

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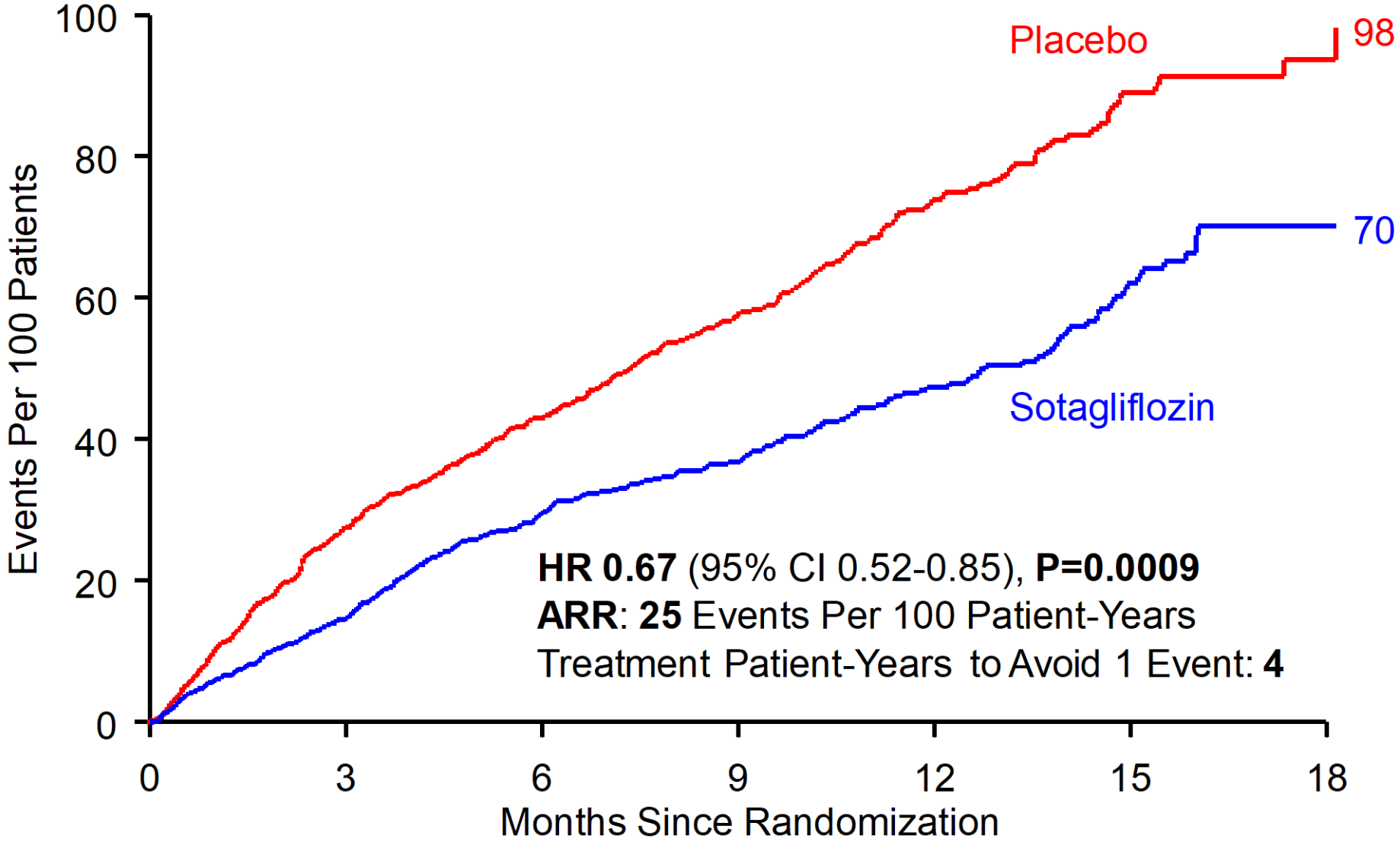
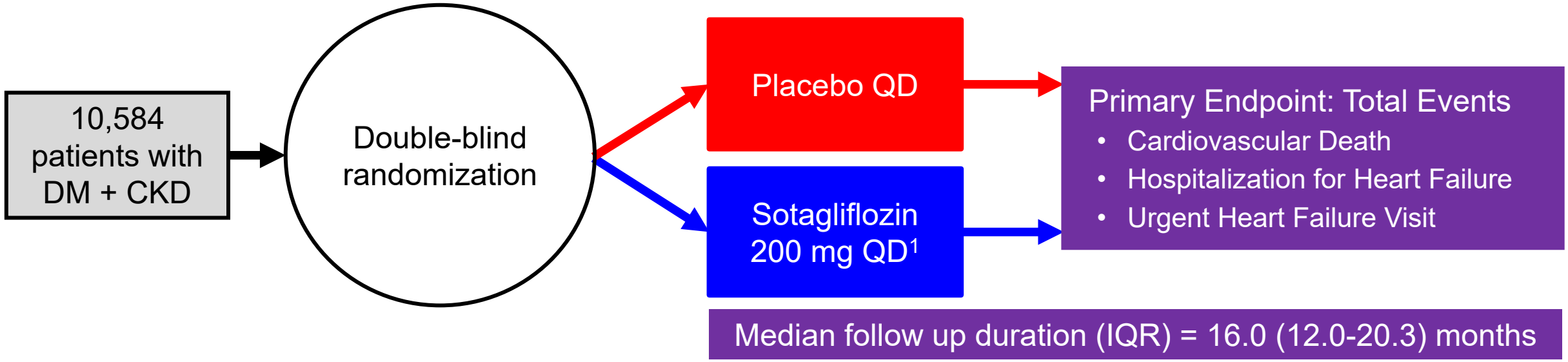


Bhatt DL, Szarek M, Steg PG, et al., and Pitt B. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.

SCORED Trial Design



Key inclusion criteria:

- Type 2 diabetes with HbA1c≥7%
- eGFR 25-60 mL/min/1.73m^2
  - with no requirement for macro- or micro-albuminuria
- CV risk factors

Key exclusion criteria:

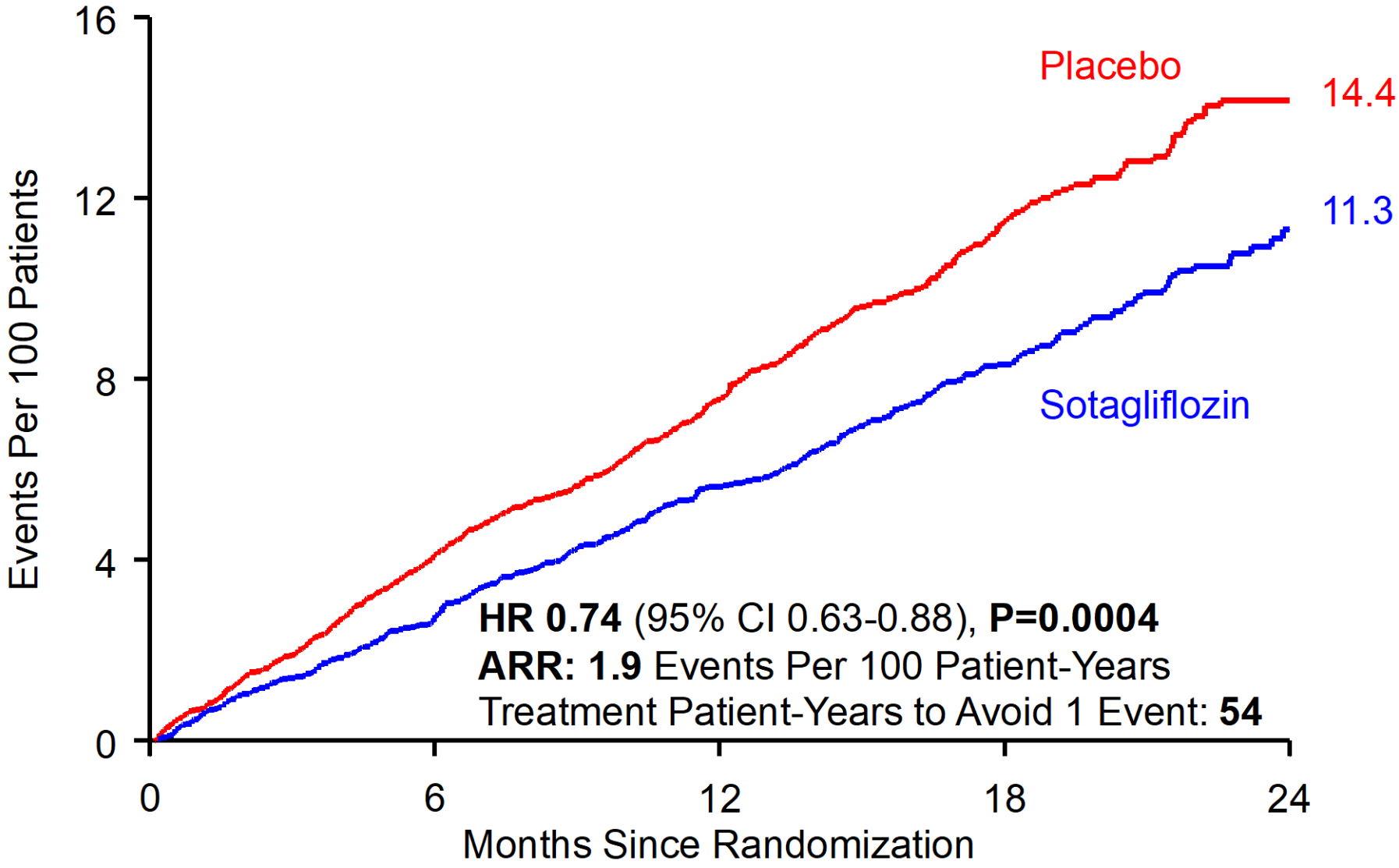
- Planned start of SGLT2 inhibitor

Bhatt DL, Szarek M, Pitt B, et al., and Steg PG. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.

[1]Goal of dose increase to 400 mg QD

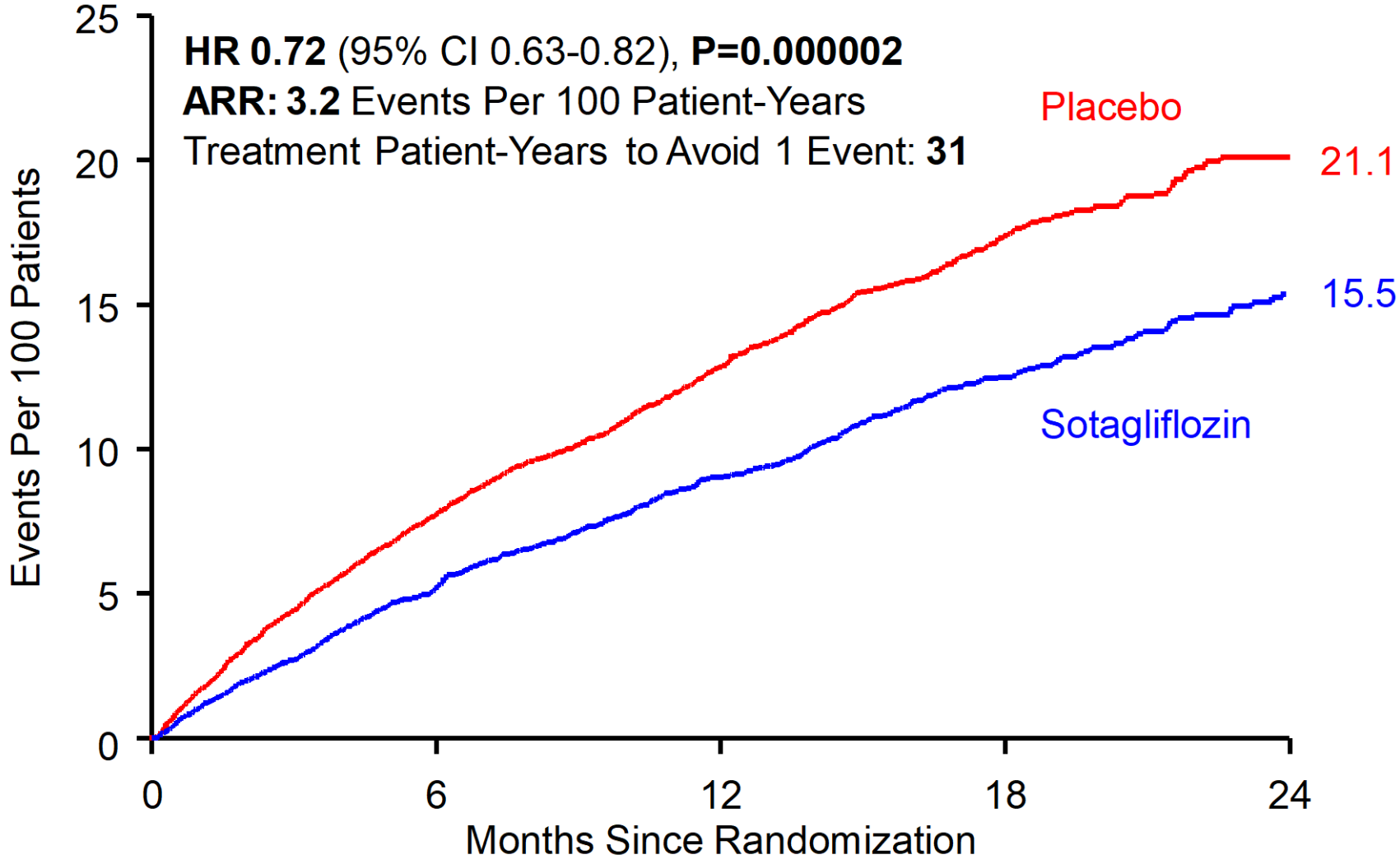
Primary Efficacy: Total CV Death, HHF, and Urgent HF Visit

SCORED



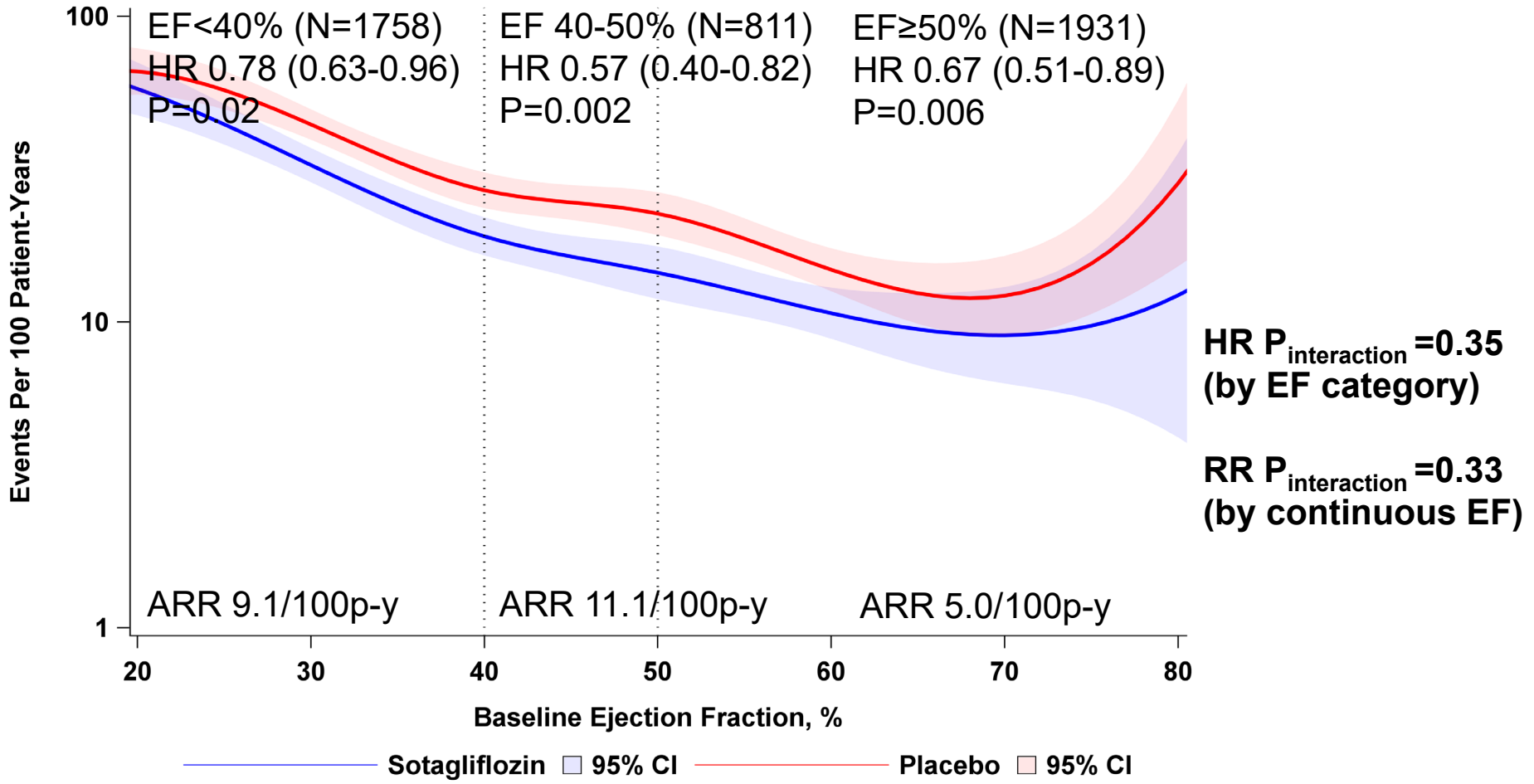
Bhatt DL, Szarek M, Pitt B, et al., and Steg PG. *N Engl J Med.* 2020. Bhatt DL. AHA 2020, virtual.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 11,806 Patients



Bhatt DL. AHA 2021, virtual.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 4,500 Patients with History of HF



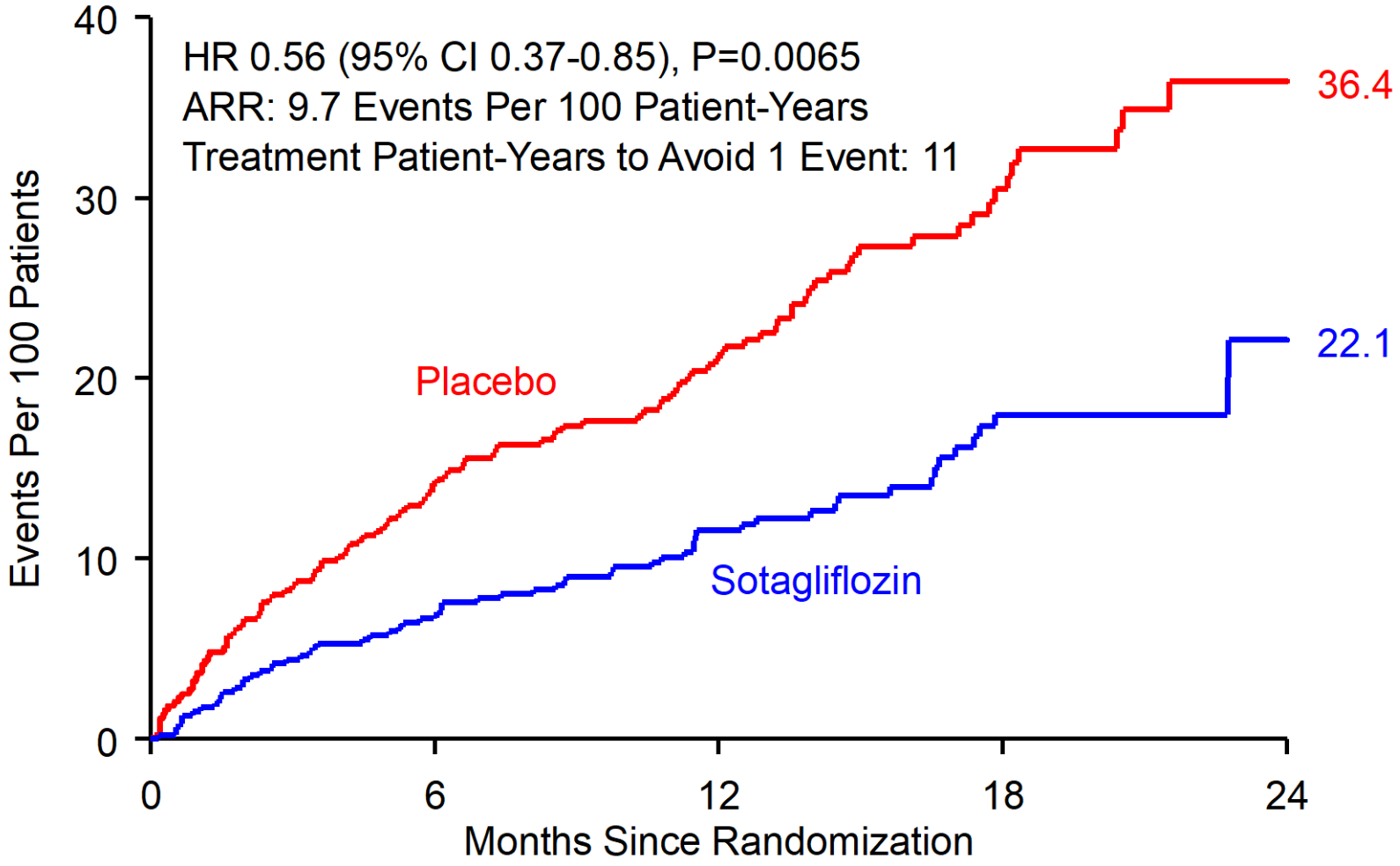
HR $P_{interaction}$ =0.35 (by EF category)

RR $P_{interaction}$ =0.33 (by continuous EF)

Bhatt DL. ACC 2021, virtual.

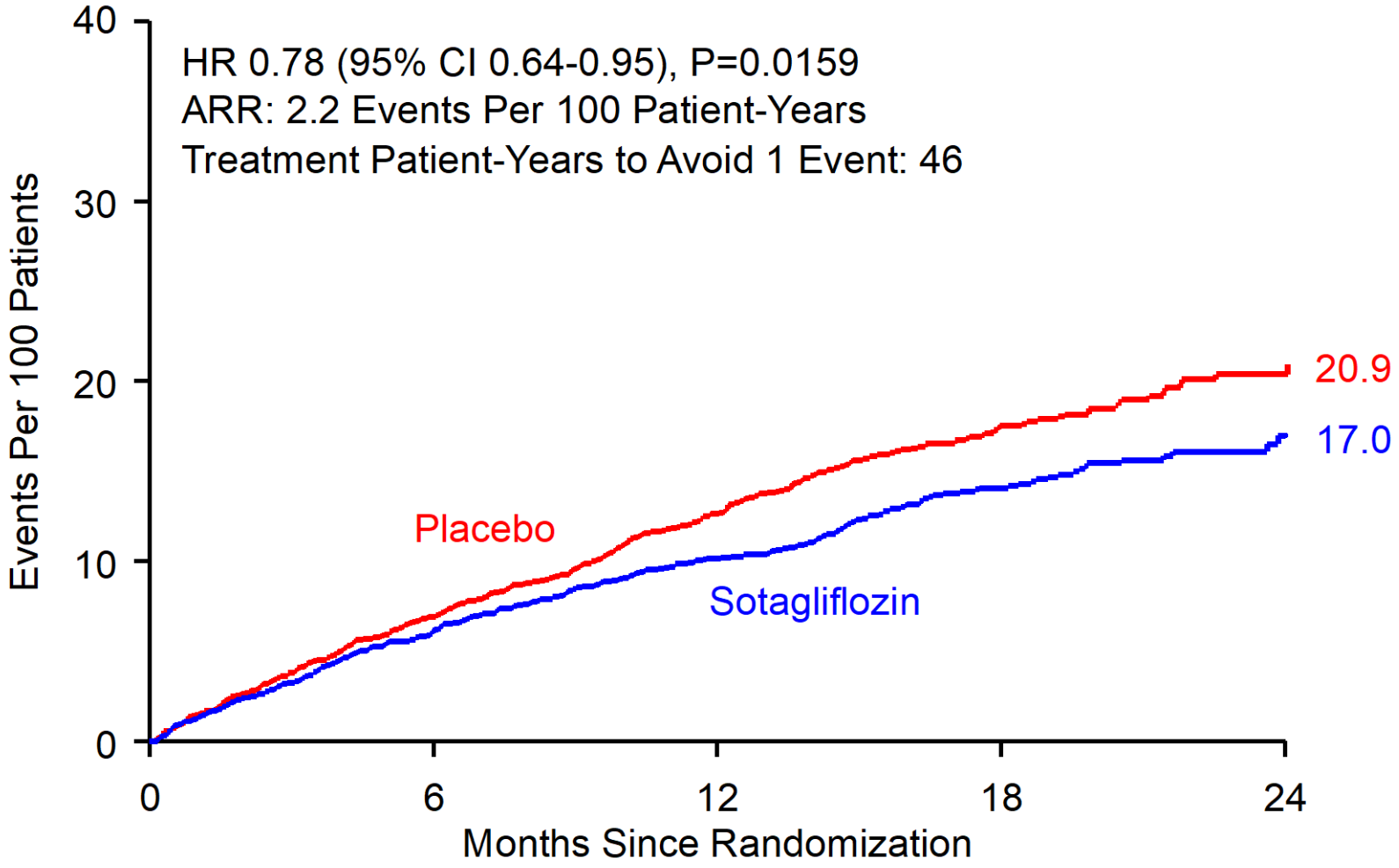
For this analysis, patients from SCORED with any history of HF are included.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 897 Patients with eGFR<30



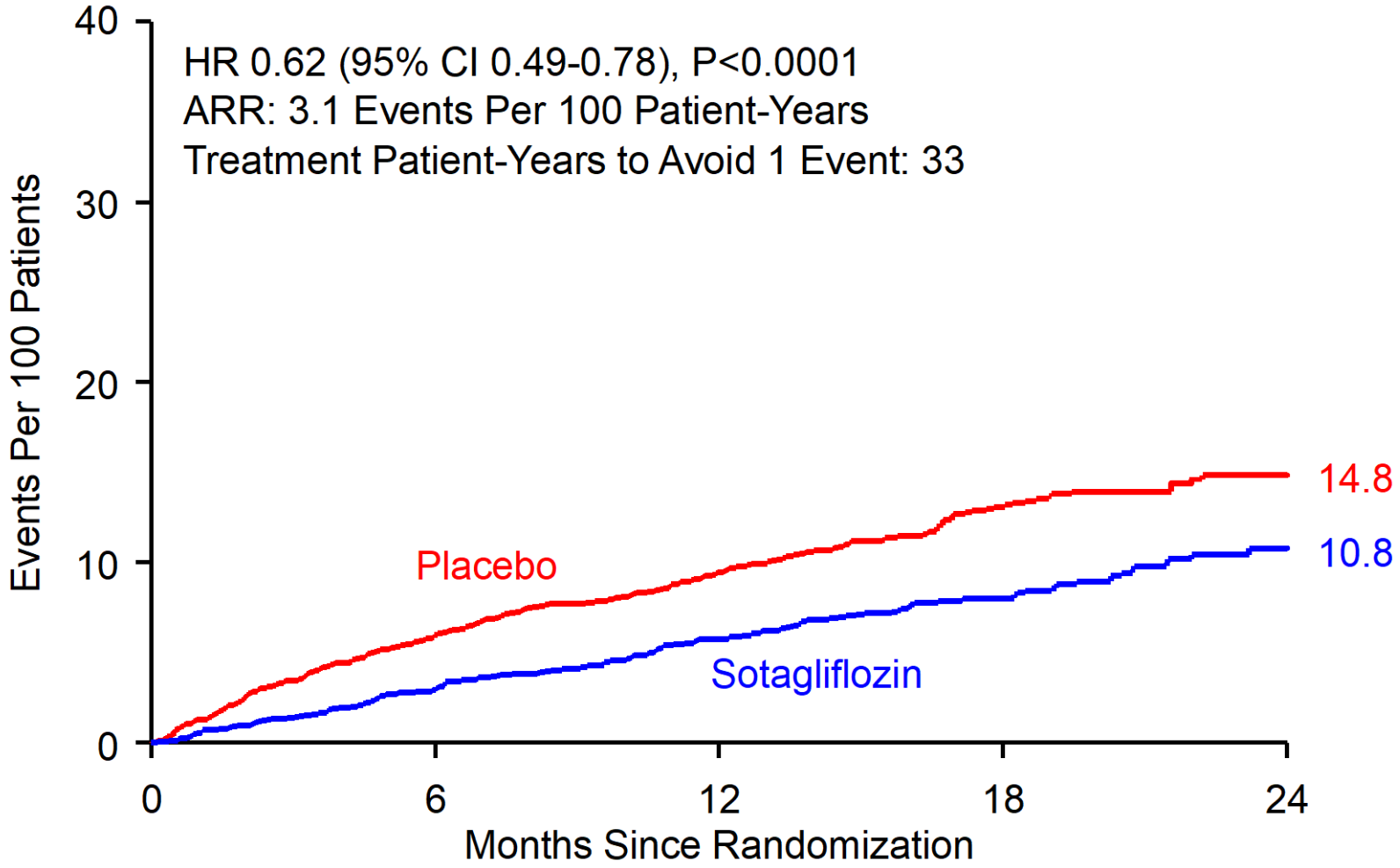
Bhatt DL. AHA 2021, virtual.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 5023 Patients with eGFR 30 to <45



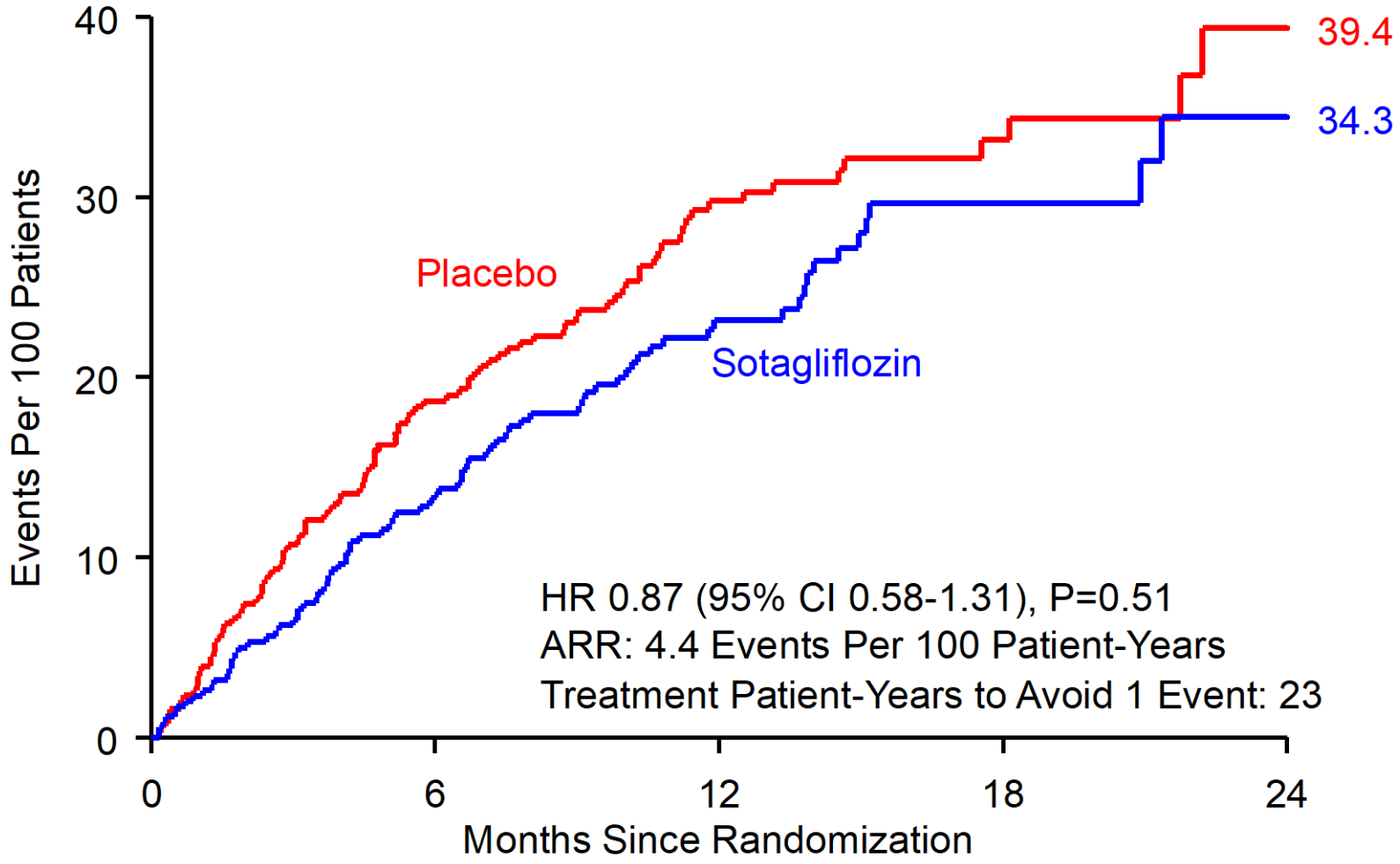
Bhatt DL. AHA 2021, virtual.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 5158 Patients with eGFR 45 to <60



Bhatt DL. AHA 2021, virtual.

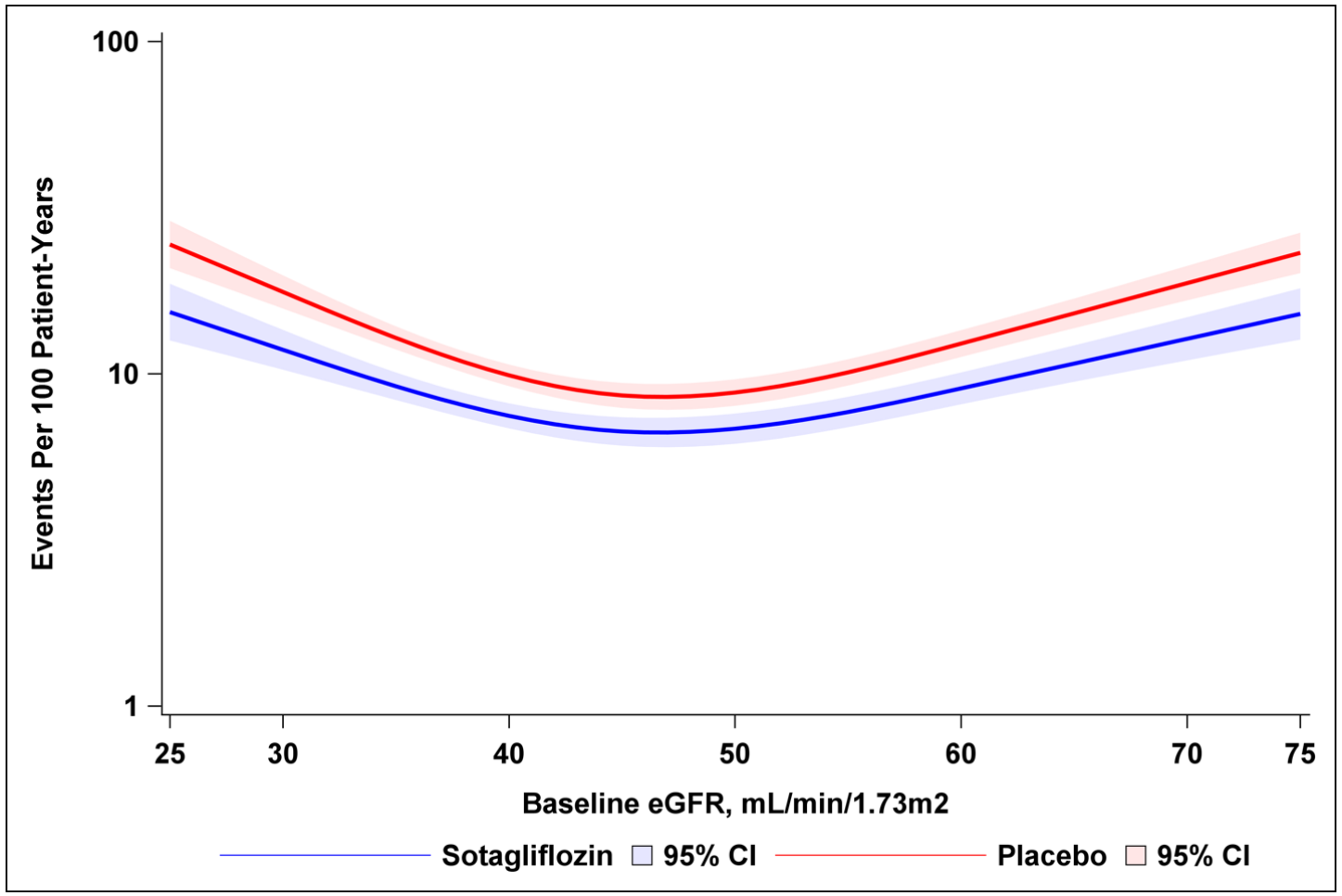
Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 728 Patients with eGFR ≥60*



Bhatt DL. AHA 2021, virtual.

*post hoc

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 11,806 Patients



Bhatt DL. AHA 2021, virtual.

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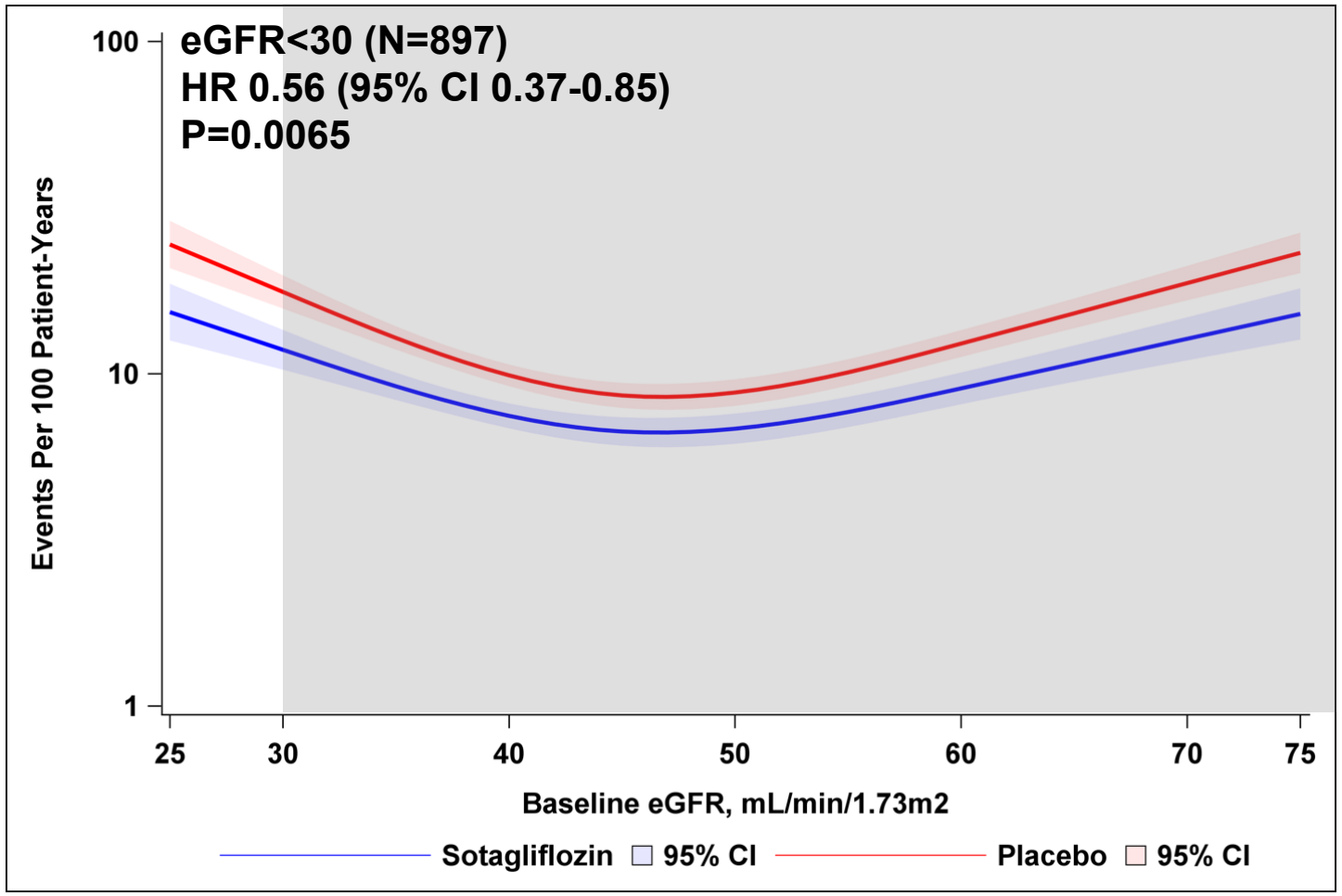

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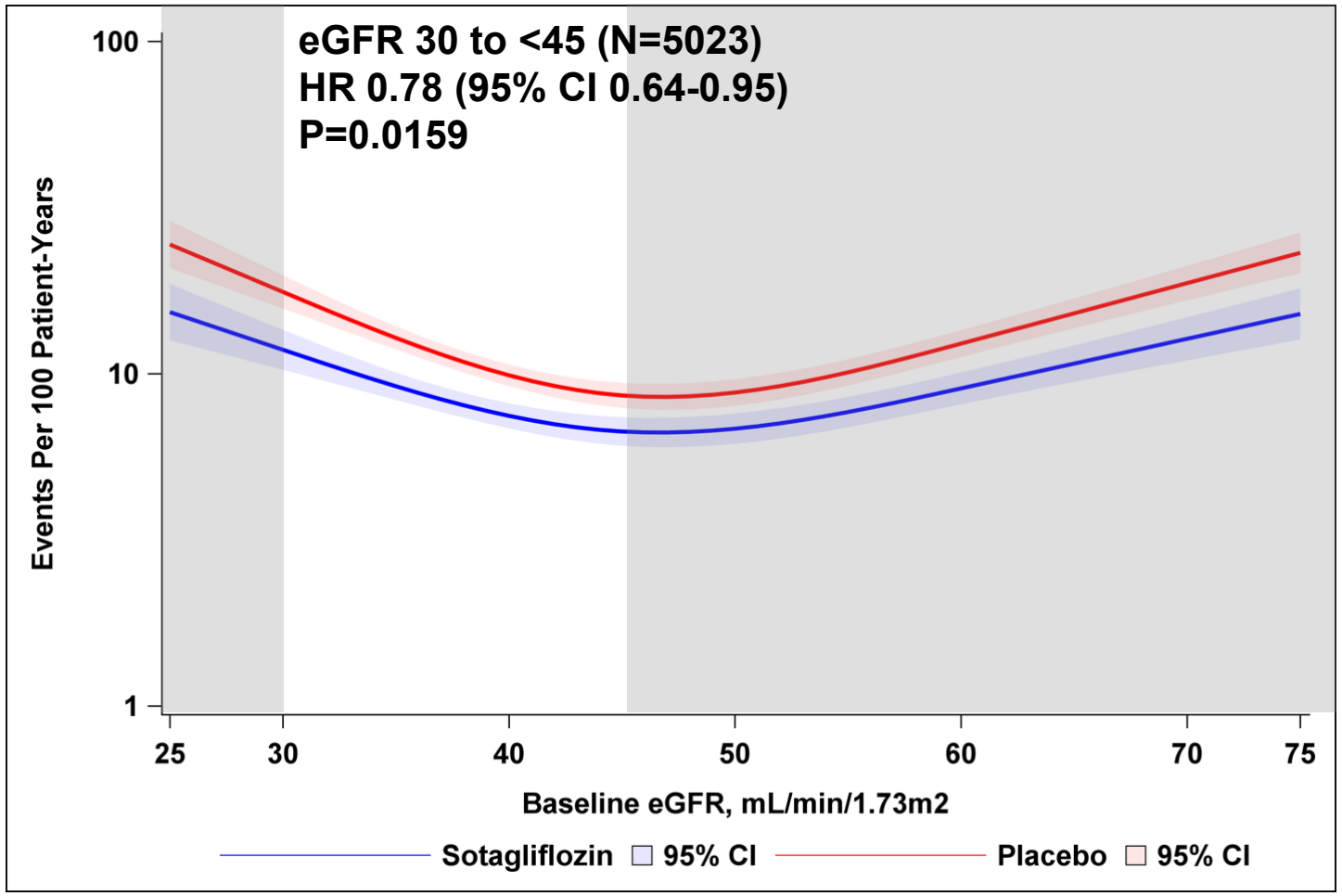

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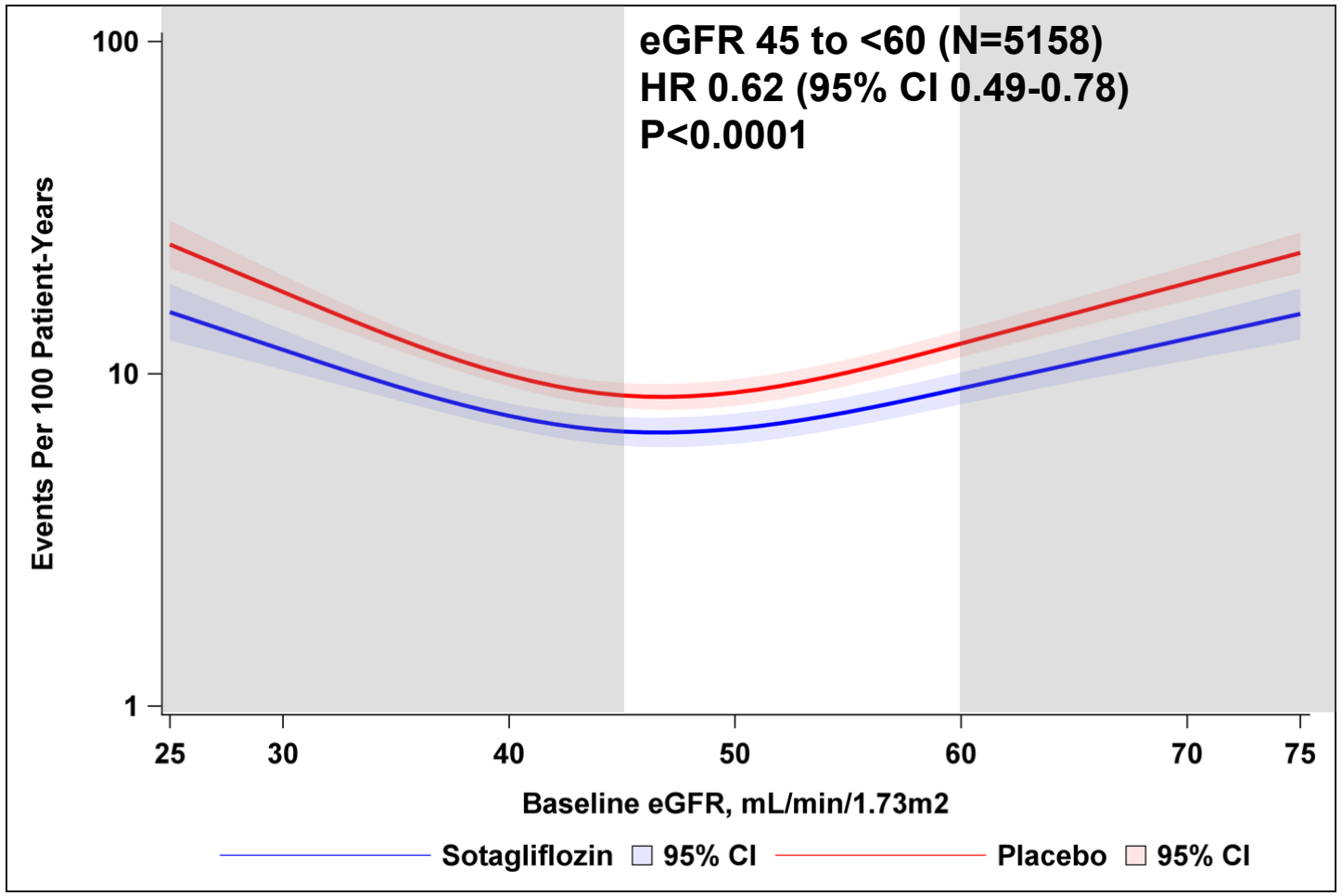
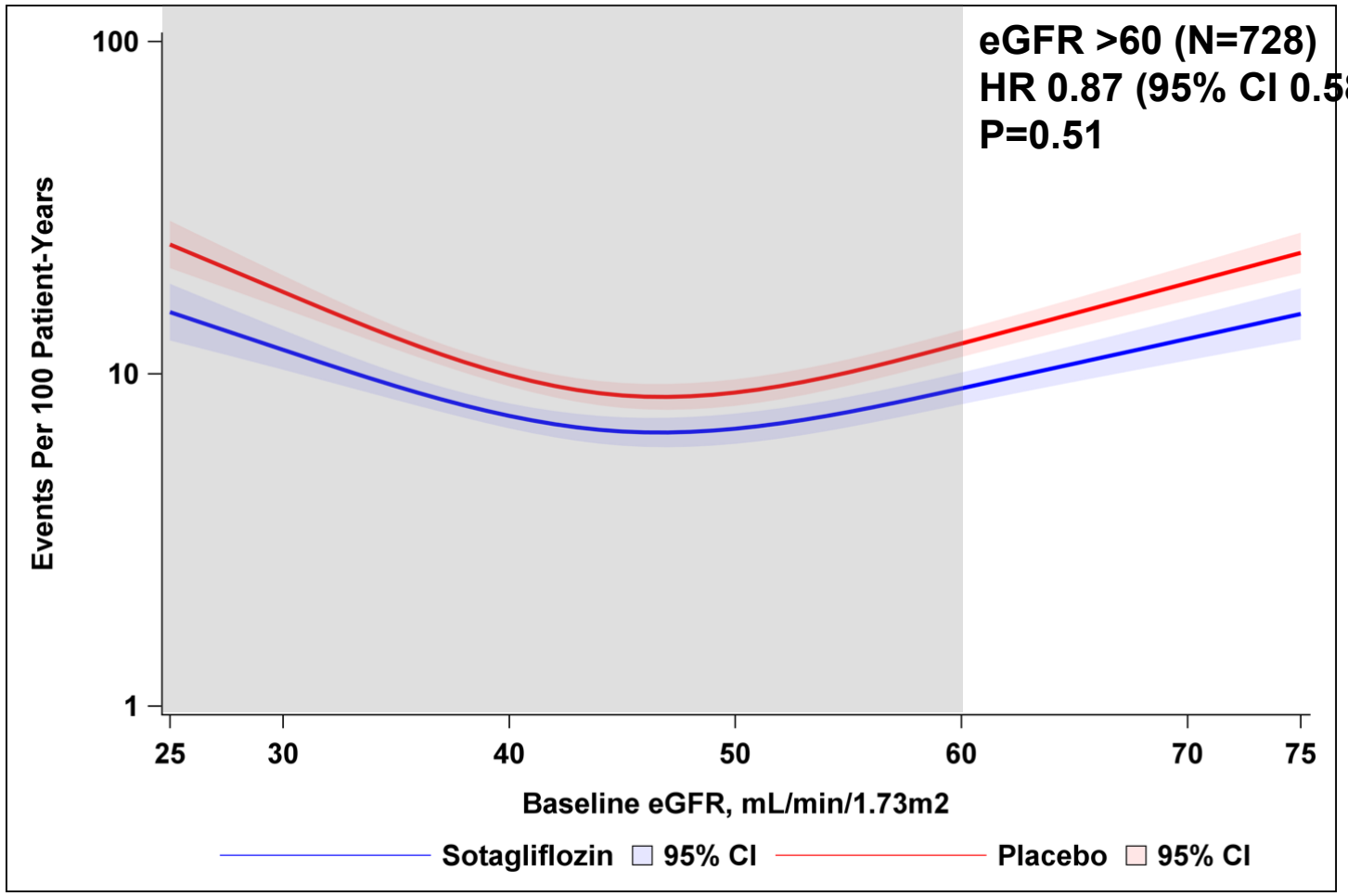


Bhatt DL. AHA 2021, virtual.

Pooled Data: SOLOIST and SCORED Total CV Death, HHF, and Urgent HF Visit in 11,806 Patients



Bhatt DL. AHA 2021, virtual.

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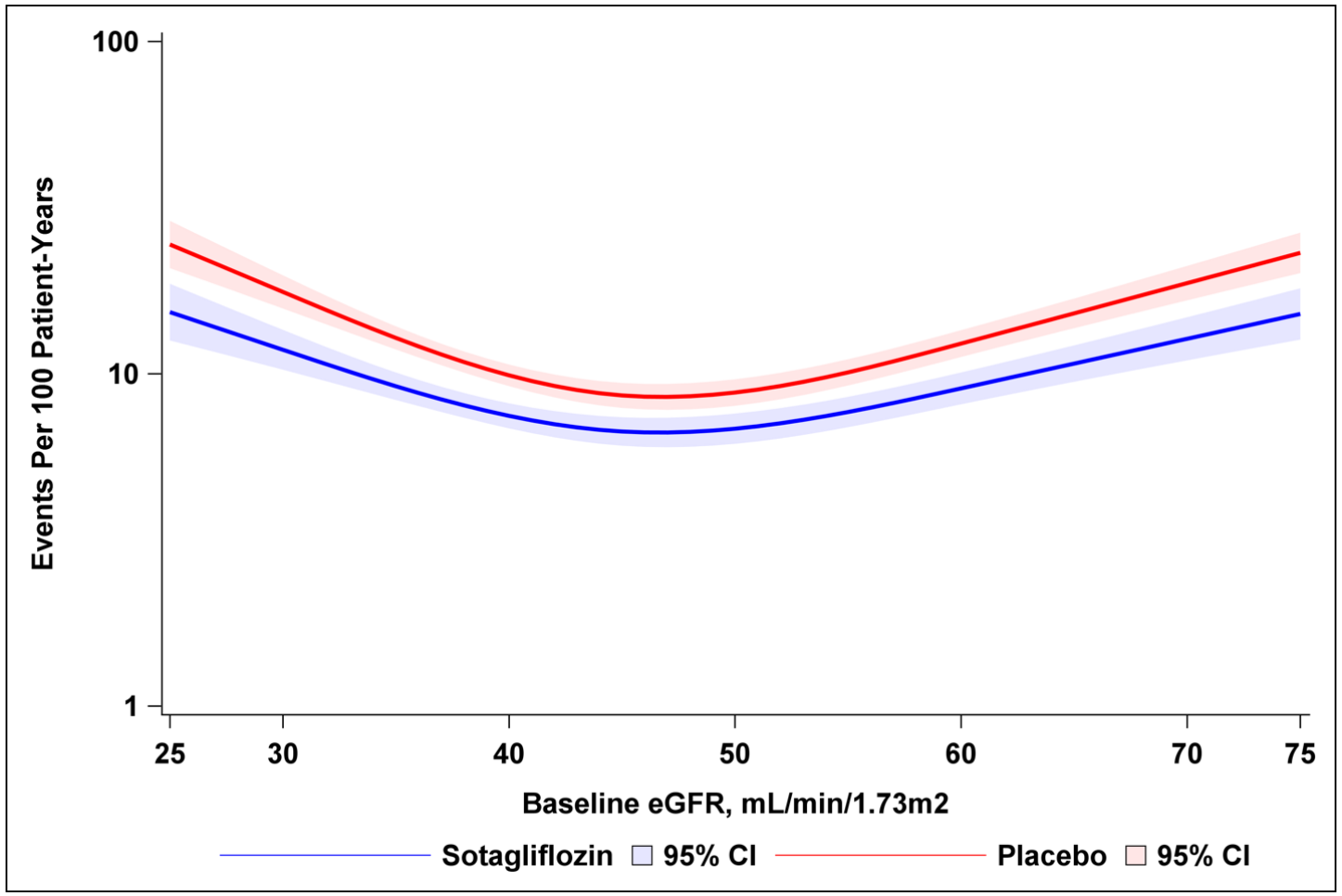
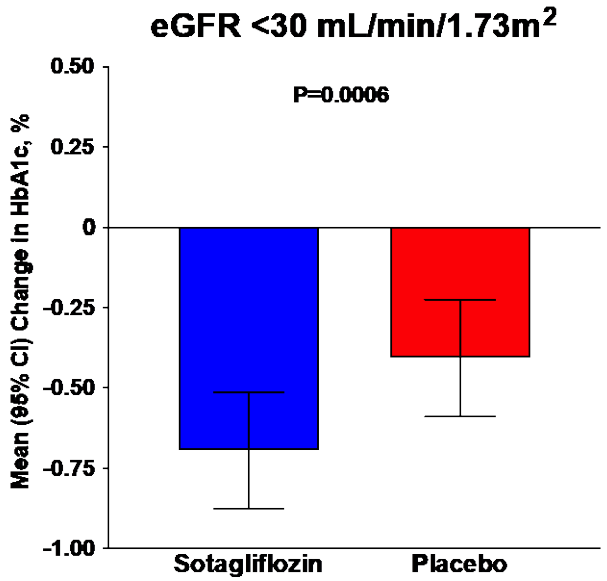


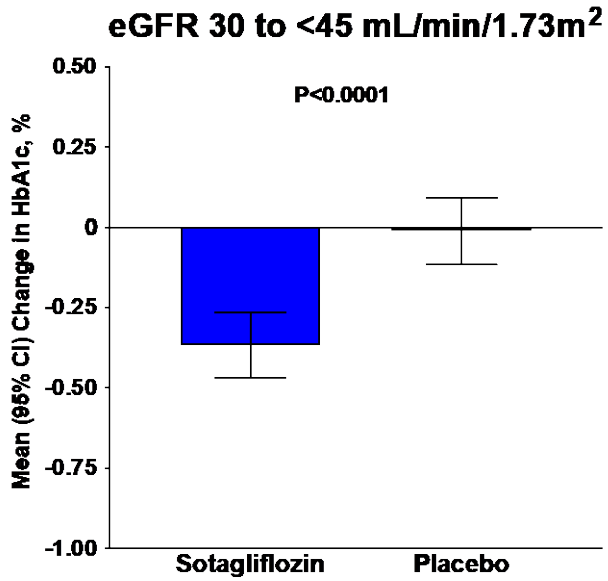
HR $P_{interaction}$ = 0.26
(3 category eGFR)

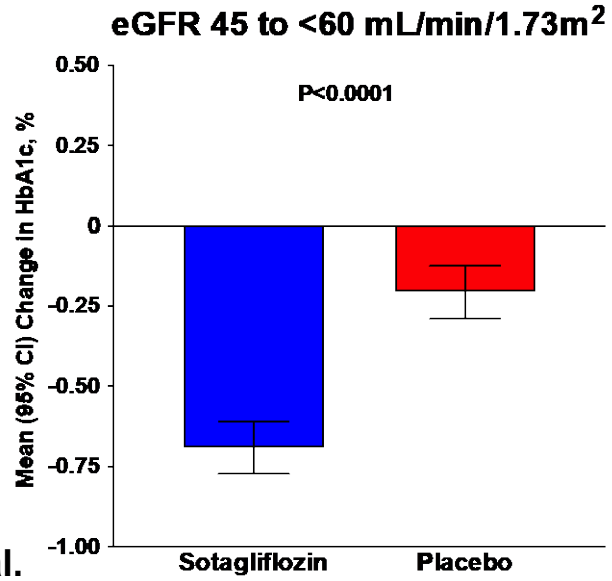
RR $P_{interaction}$ = 0.20
(continuous eGFR)

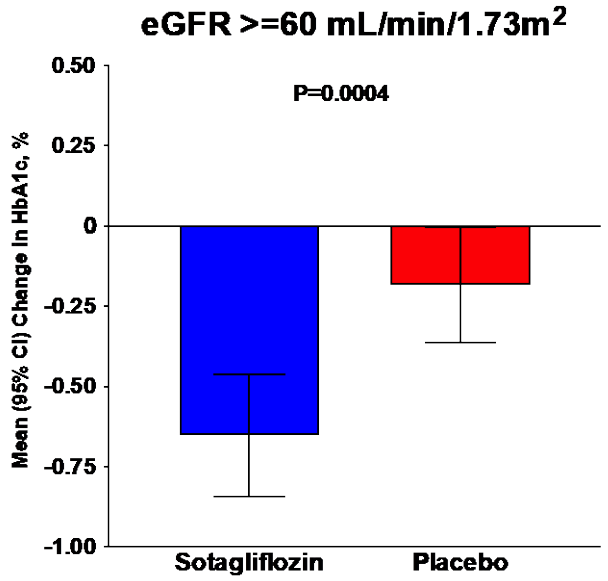
Bhatt DL. AHA 2021, virtual.

Pooled Data: SOLOIST and SCORED HbA1c Across eGFR in 11,806 Patients









Bhatt DL. AHA 2021, virtual.

Limitations

SOLOIST SCORED

Trials were stopped early

- Nevertheless, robust reduction in primary endpoint in each trial

Most of the present analyses were prespecified, though the eGFR ≥60 analysis was *post hoc*

- However, both types of analyses were consistent in terms of demonstrating benefits

Conclusions

SOLOIST SCORED

Sotagliflozin robustly and significantly reduced the composite of total cardiovascular deaths, hospitalizations for heart failure, and urgent visits for heart failure across the full range of kidney function studied.

This adds to prior analyses that have demonstrated the benefits of **sotagliflozin** across the full range of EF, including normal EF.

Furthermore, **sotagliflozin** reduced hemoglobin A1c across the full range of eGFR studied, and, unlike other SGLT2 inhibitors, including in patients with very low eGFR.

BRIGHAM AND WOMEN'S HOSPITAL

Heart & Vascular Center

Thank You!

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