DukeHeart *On The Go*

Sotagliflozin in Patients with Diabetes and Chronic Kidney Disease – The SCORED Trial

SCORED

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Disclosures

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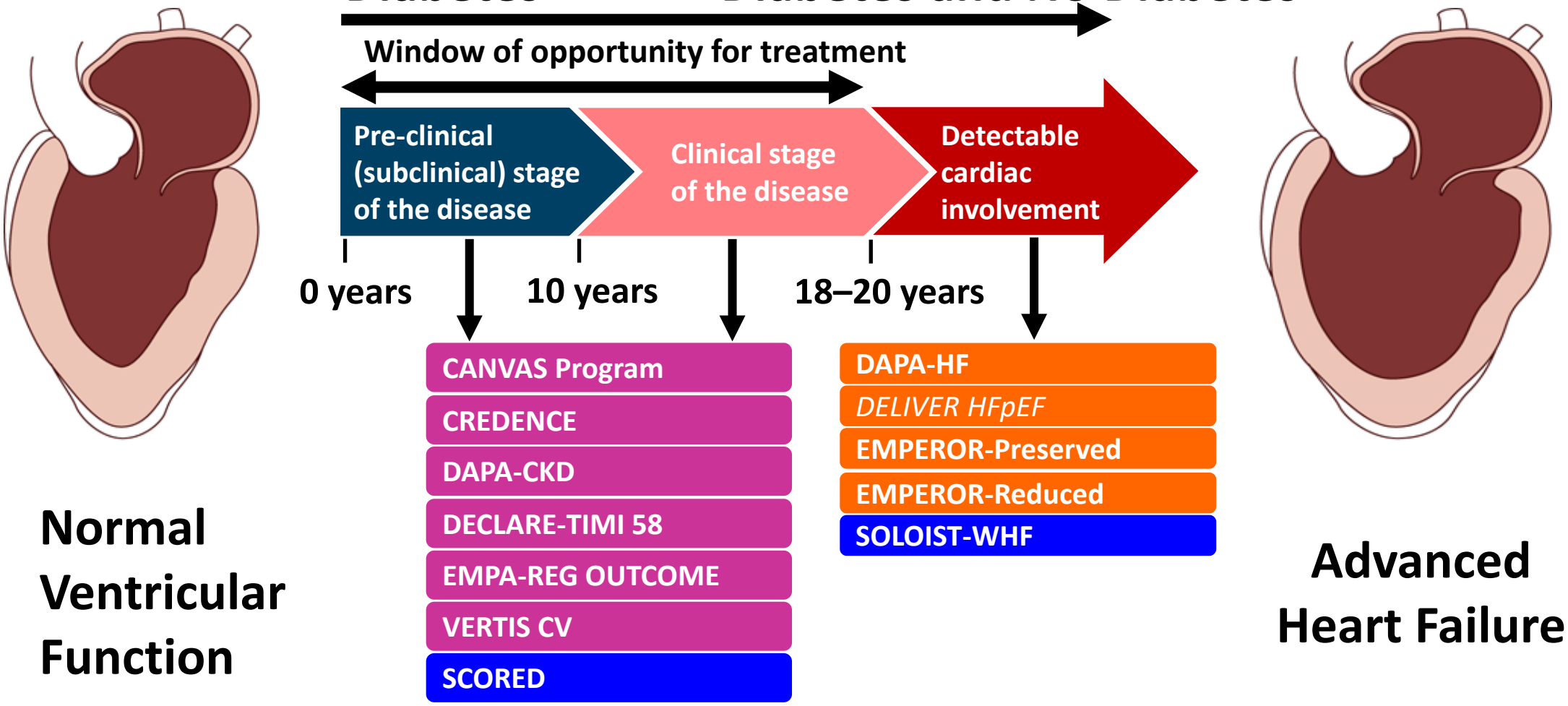
SCORED was initially sponsored by Sanofi and then by Lexicon.

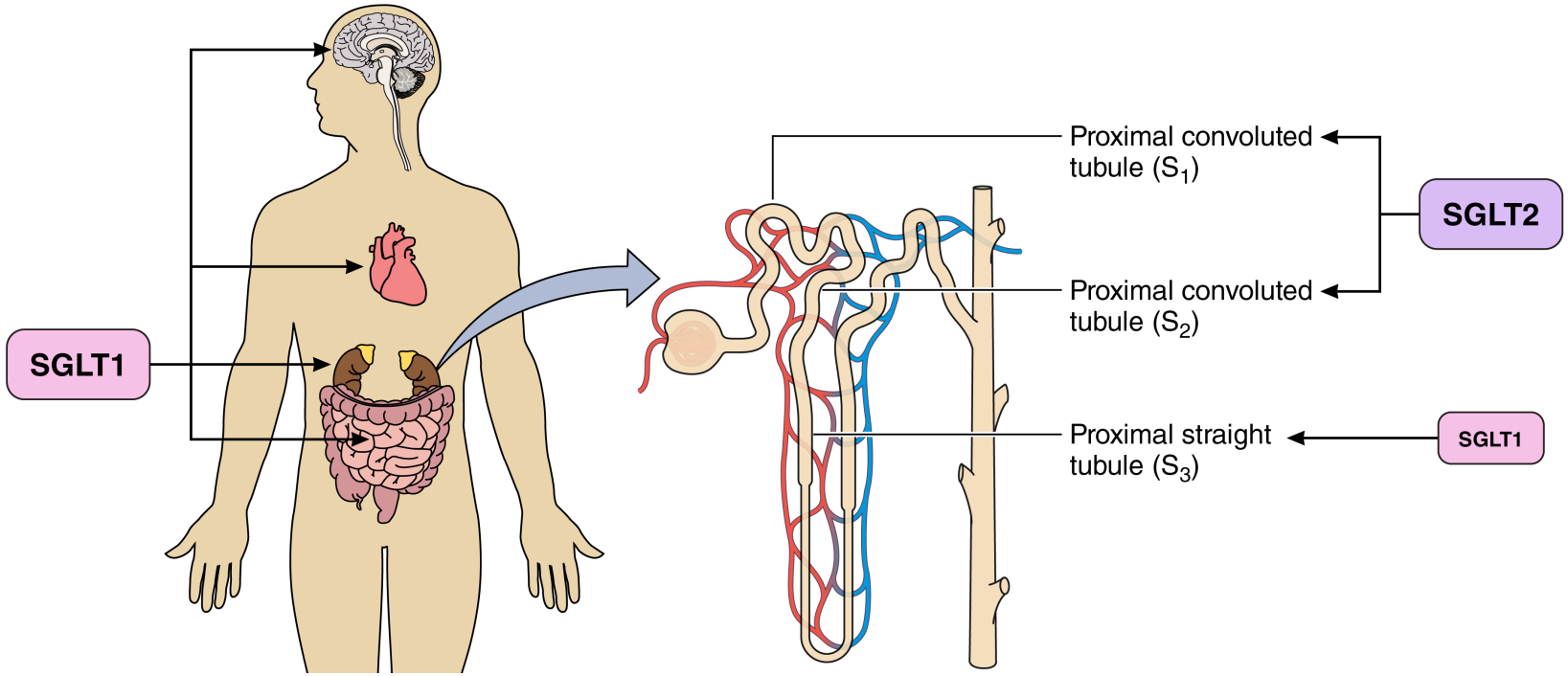
This presentation includes the off-label and investigational uses of drugs.

The Evolution of SGLT2i in Heart Failure Management



Adapted from Bhatt DL, et al. *Cell Metabolism.* 2019;30(5):847-849.

Sotagliflozin: Dual SGLT1 and SGLT2 Inhibitor

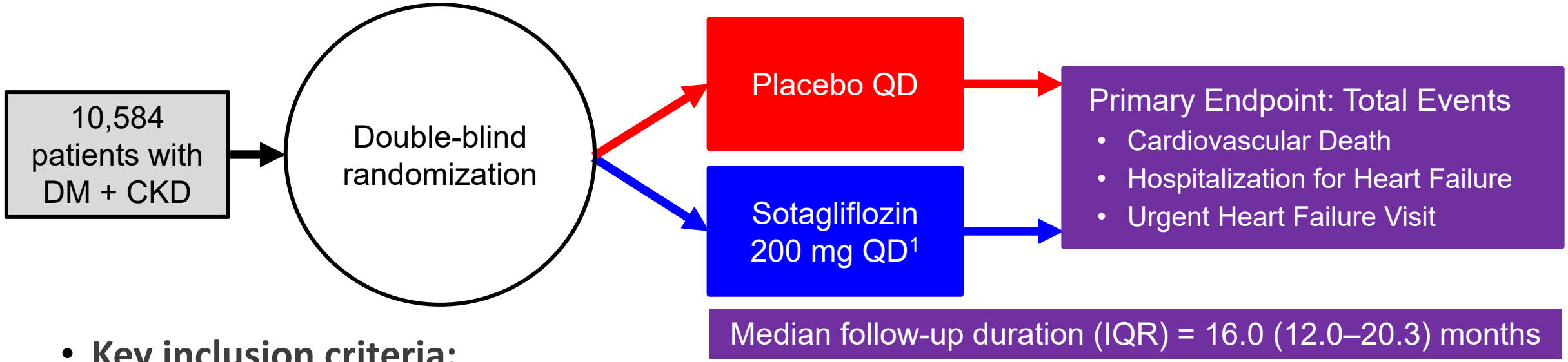


- **SGLT1** is the primary transporter for absorption of glucose and galactose in the GI tract
- Pharmacologic inhibition by sotagliflozin is independent of insulin and does not depend on kidney function
- Potential reduction in atherosclerotic risks

- **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, et al. *Circulation.* 2021;144(1):4-6.

SCORED Trial Design

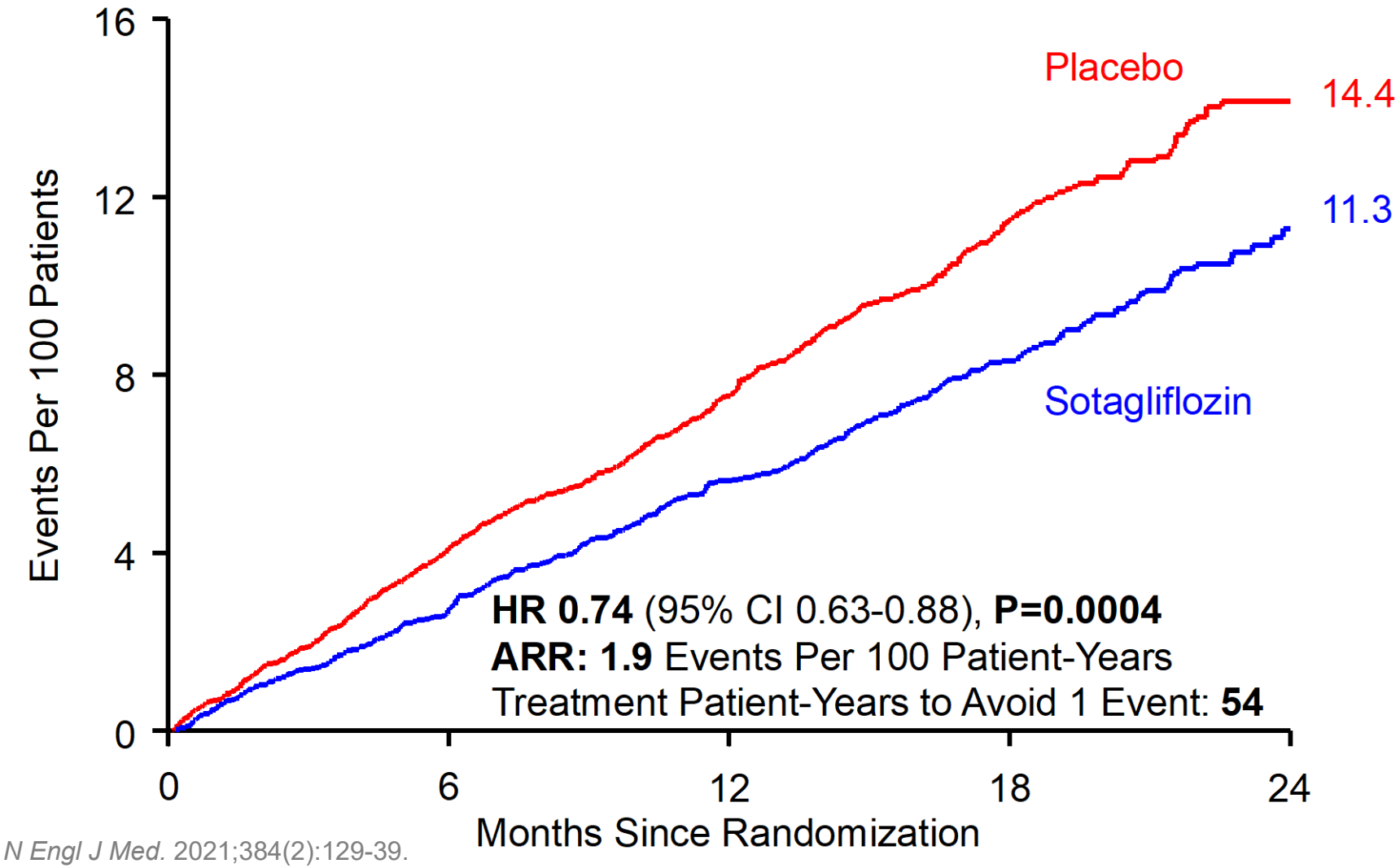


- **Key inclusion criteria:**
  - Type 2 diabetes with HbA1c ≥ 7%
  - eGFR 25–60 mL/min/1.73m2
    – with no requirement for macro- or micro-albuminuria
  - CV risk factors
- **Key exclusion criteria:**
  - Planned start of SGLT2 inhibitor

Bhatt DL, et al. *N Engl J Med.* 2021;384(2):117-128.
Bhatt DL, AHA 2020. Virtual.

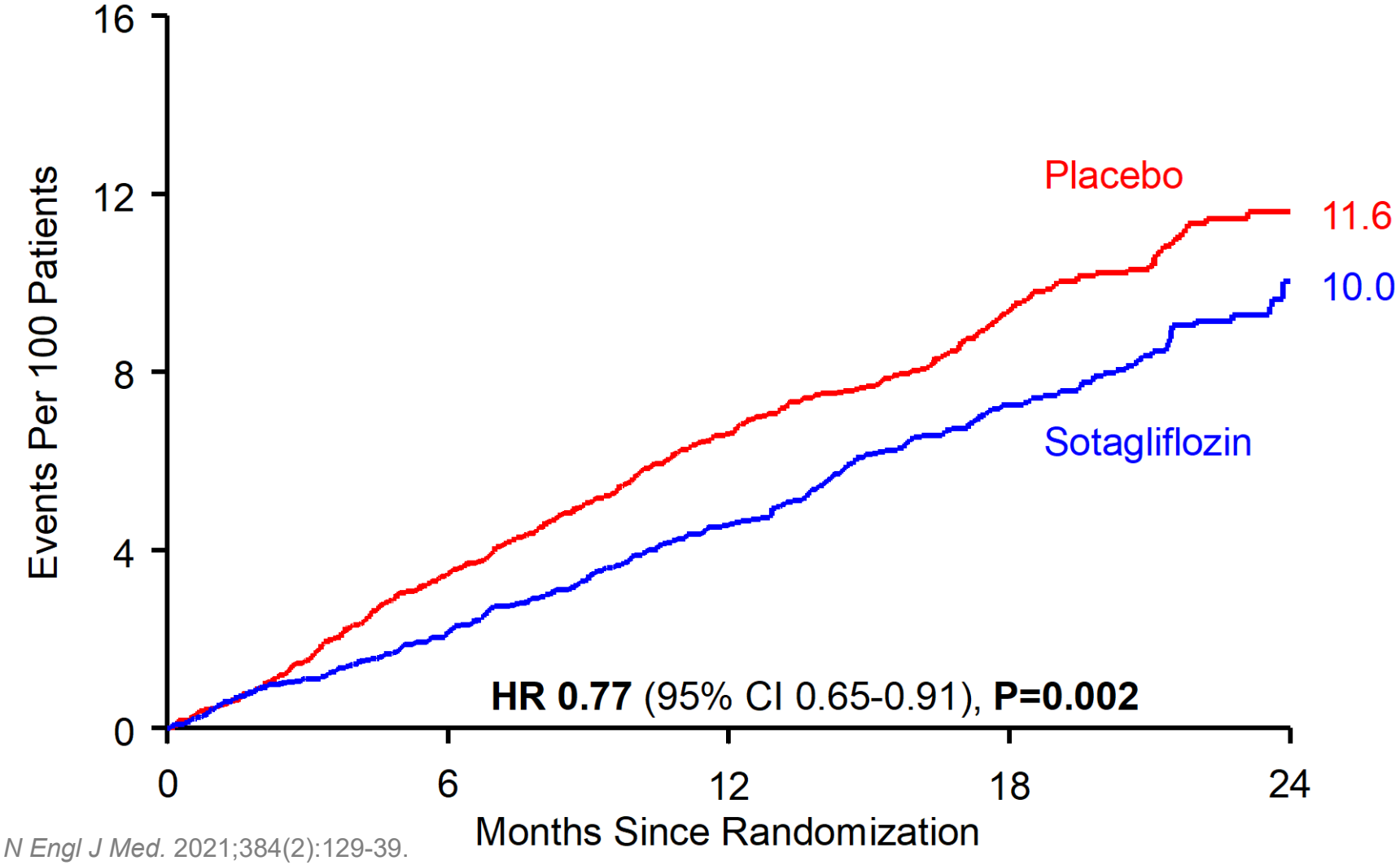
[1]Goal of dose increase to 400 mg QD

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



Bhatt DL, et al. *N Engl J Med.* 2021;384(2):129-39.
Bhatt DL, AHA 2020. Virtual.

Total CV Death, Non-Fatal MI, or Non-Fatal Stroke



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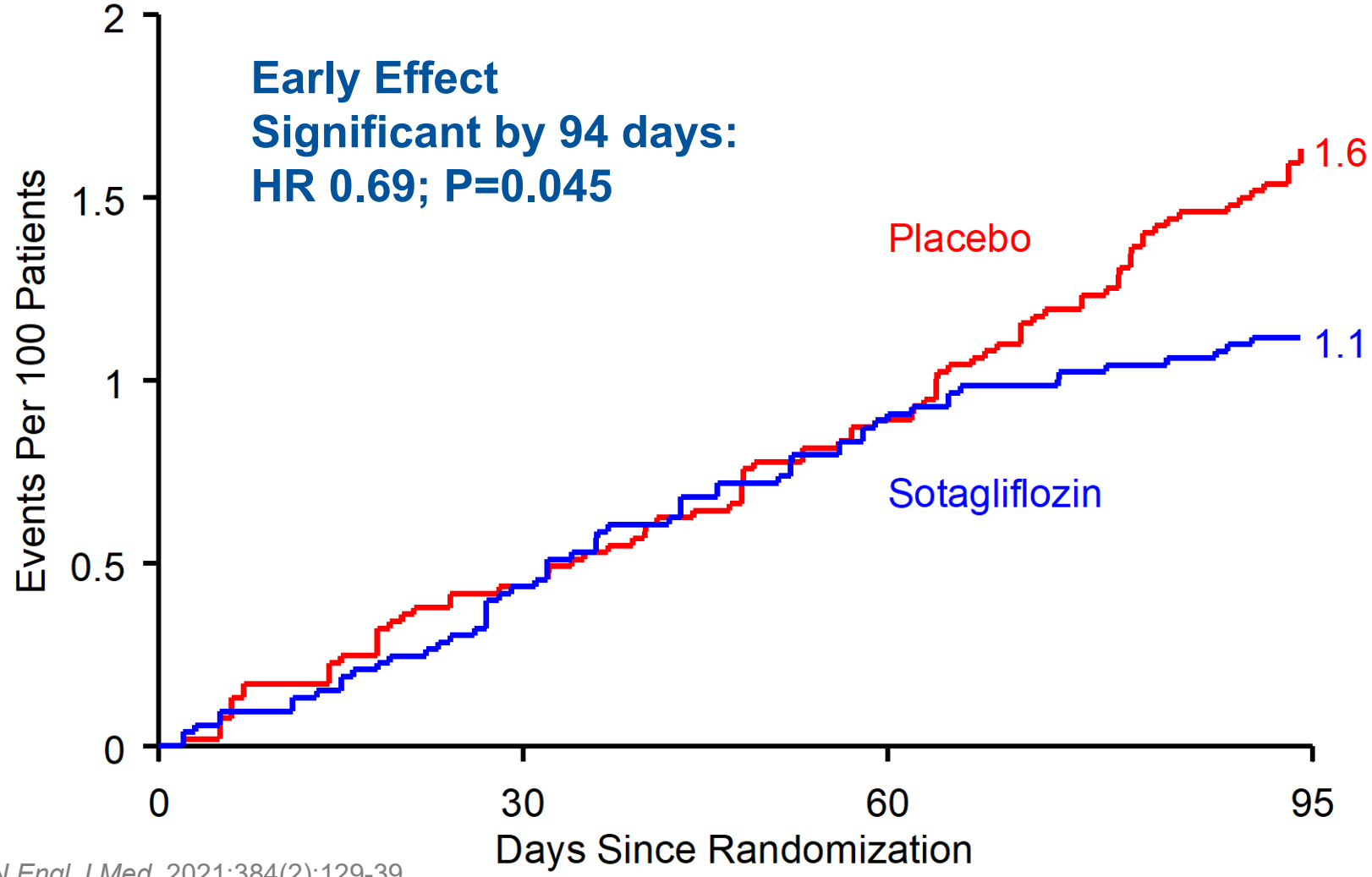
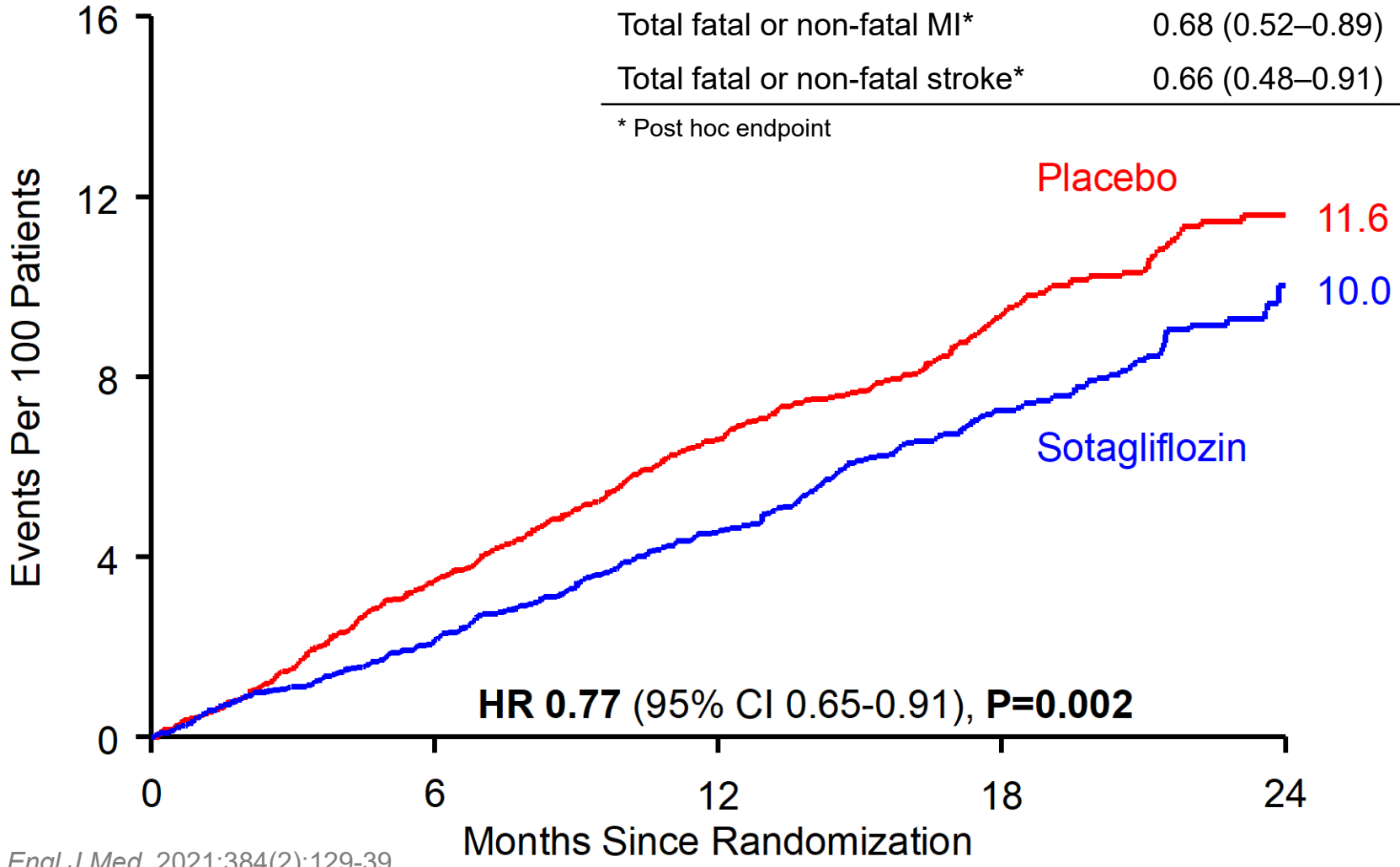


Bhatt DL, et al. *N Engl J Med.* 2021;384(2):129-39.
Bhatt DL, AHA 2020. Virtual.

Total CV Death, Non-Fatal MI, or Non-Fatal Stroke

Endpoint	HR (95%CI)	P-value
Total fatal or non-fatal MI*	0.68 (0.52–0.89)	0.004
Total fatal or non-fatal stroke*	0.66 (0.48–0.91)	0.012

* Post hoc endpoint



Bhatt DL, et al. *N Engl J Med.* 2021;384(2):129-39.
Bhatt DL, AHA 2020. Virtual.

History of Cardiovascular Disease (CVD) Subgroup Analyses

Subgroups

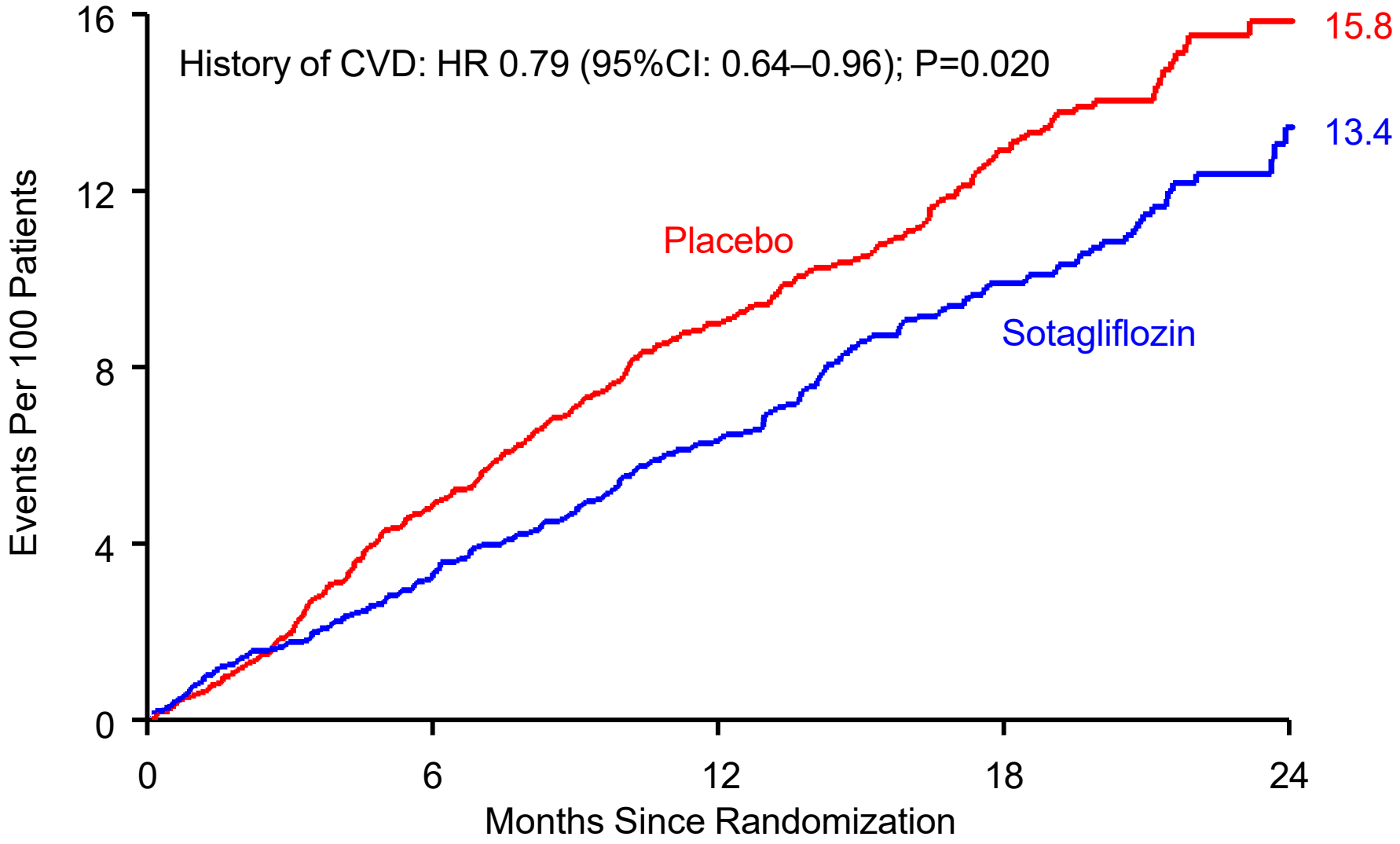
- History of cardiovascular disease at baseline (N=5144 patients)
- No history of cardiovascular disease at baseline (N=5440 patients)

The prespecified definition of history of CVD included prior myocardial infarction, prior stroke, coronary revascularization, and peripheral vascular disease; (multiple post hoc sensitivity analyses yielded similar results)

Endpoints

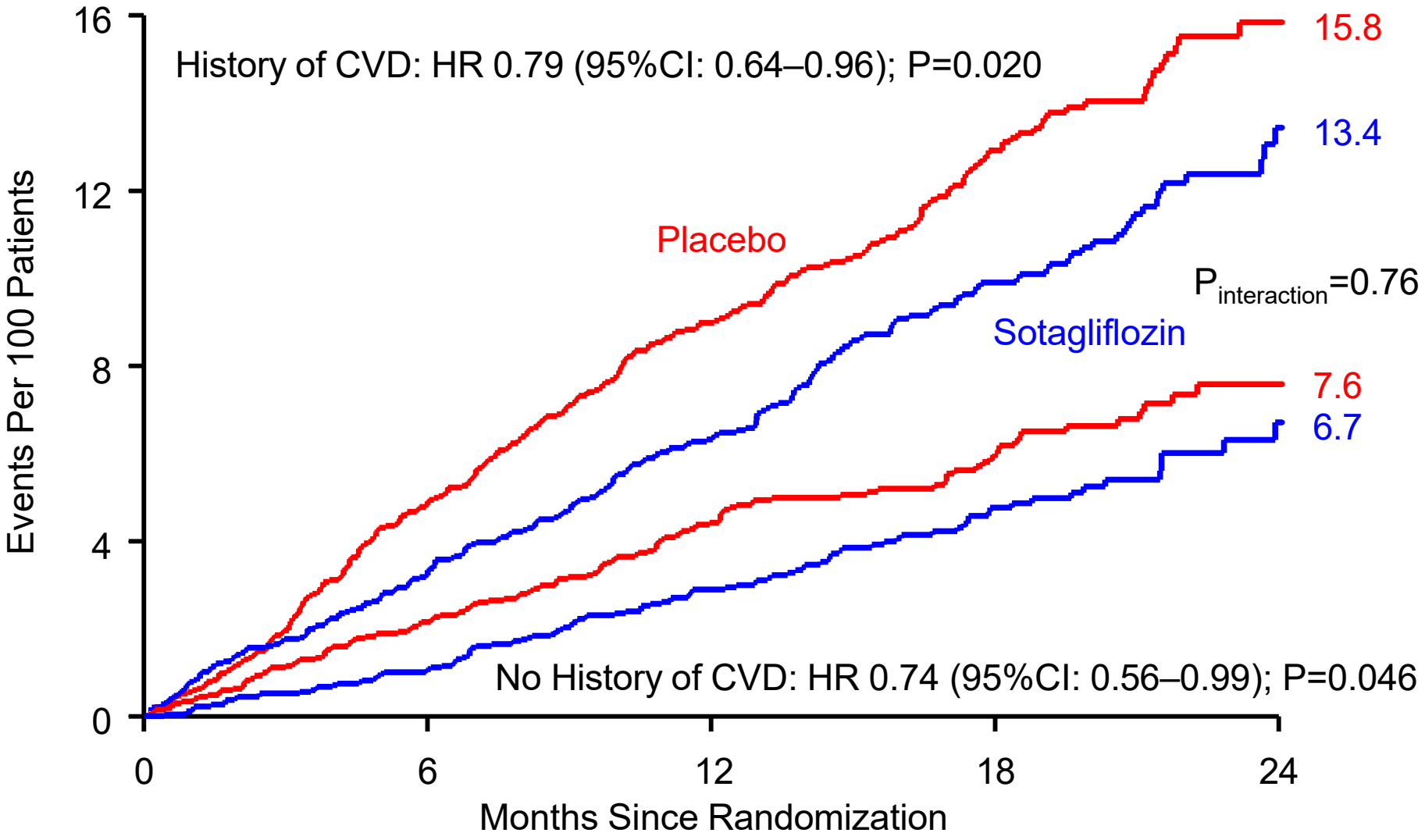
- Total MACE (first and recurrent events)
- Total MI (fatal and non-fatal MI)
- Total stroke (fatal and non-fatal stroke)

Total CV Death, Non-Fatal MI, or Non-Fatal Stroke by CVD Subgroup



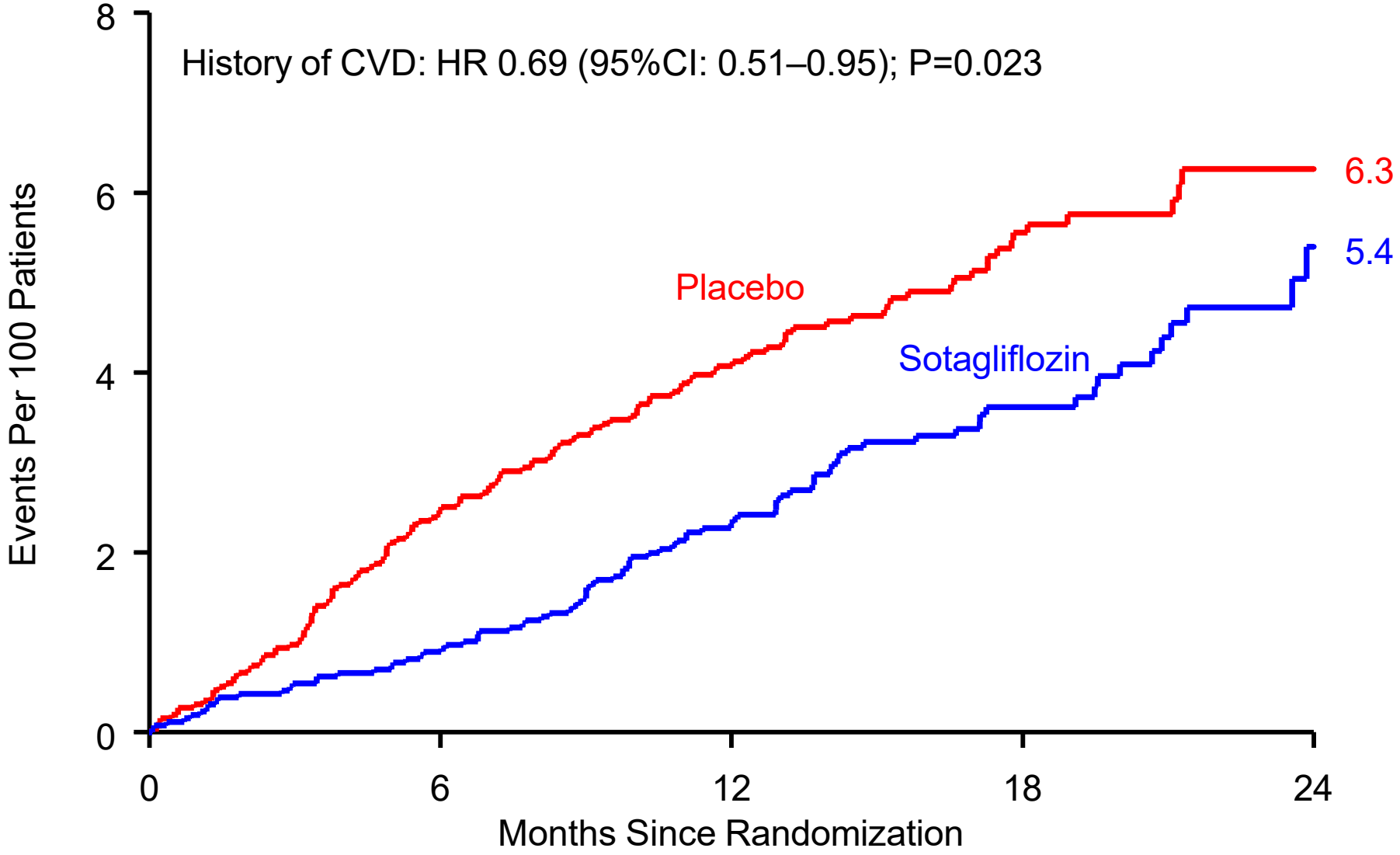
Bhatt DL, ACC 2022.

Total CV Death, Non-Fatal MI, or Non-Fatal Stroke by CVD Subgroup



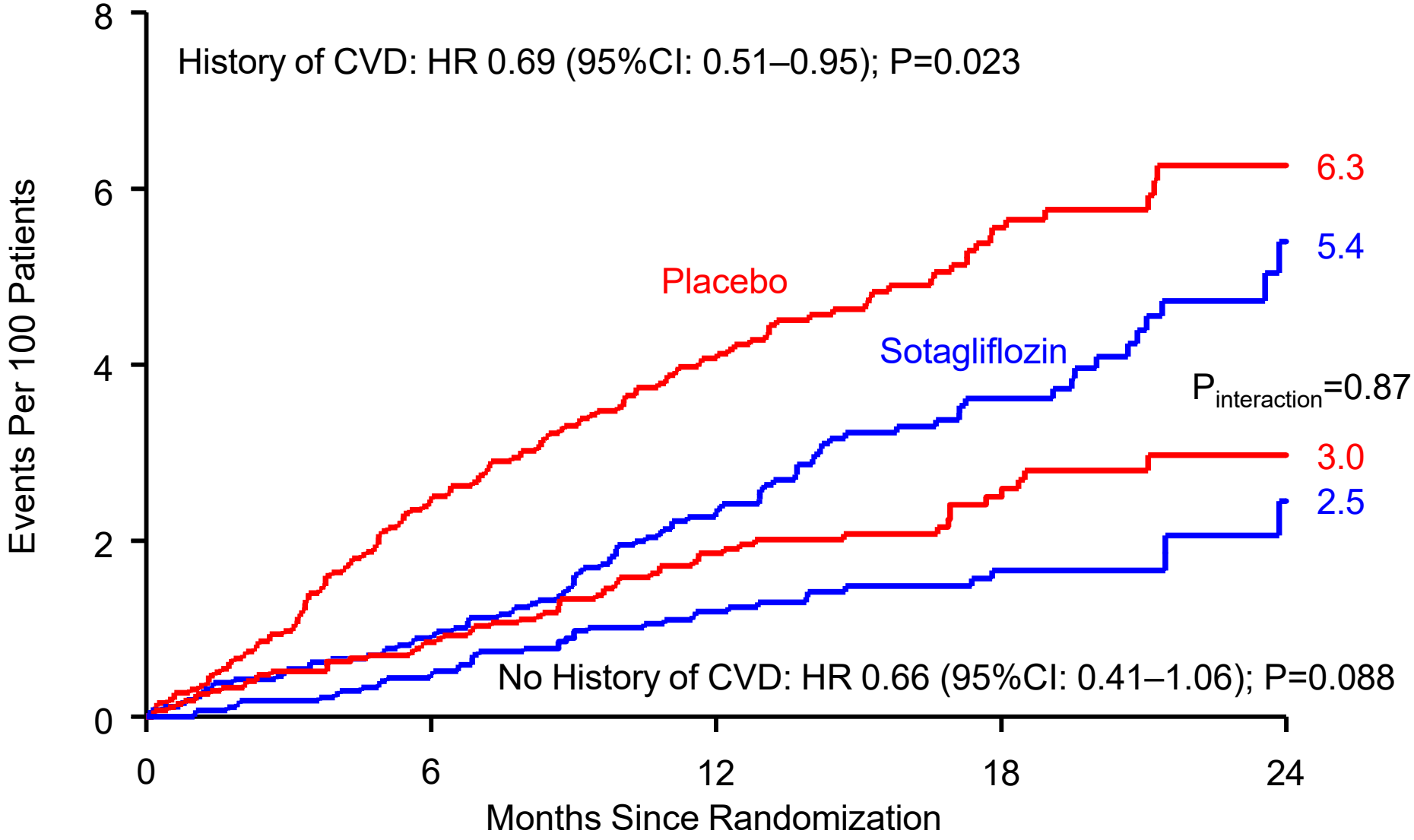
Bhatt DL, ACC 2022.

Total MI by CVD Subgroup



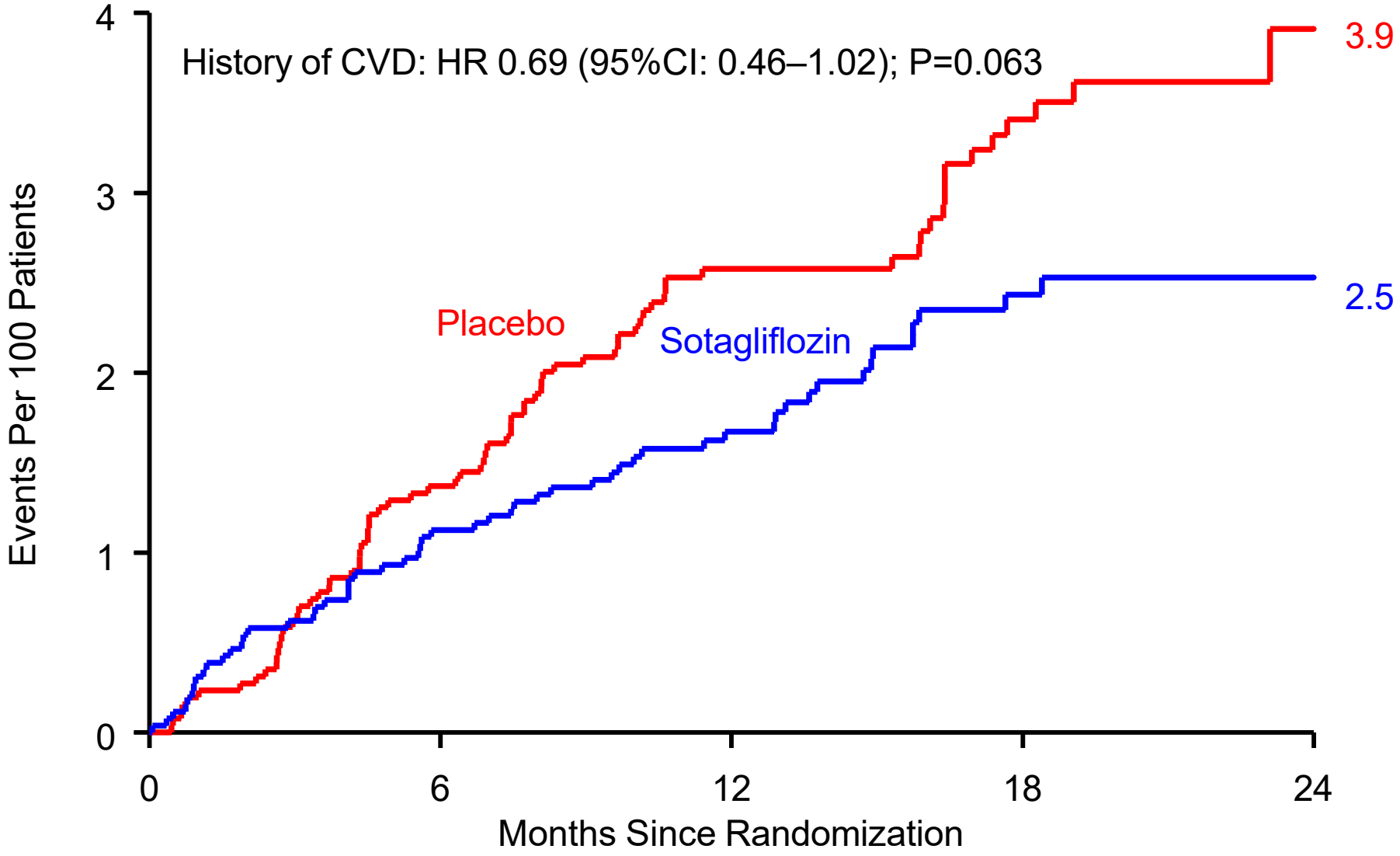
Bhatt DL, ACC 2022.

Total MI by CVD Subgroup



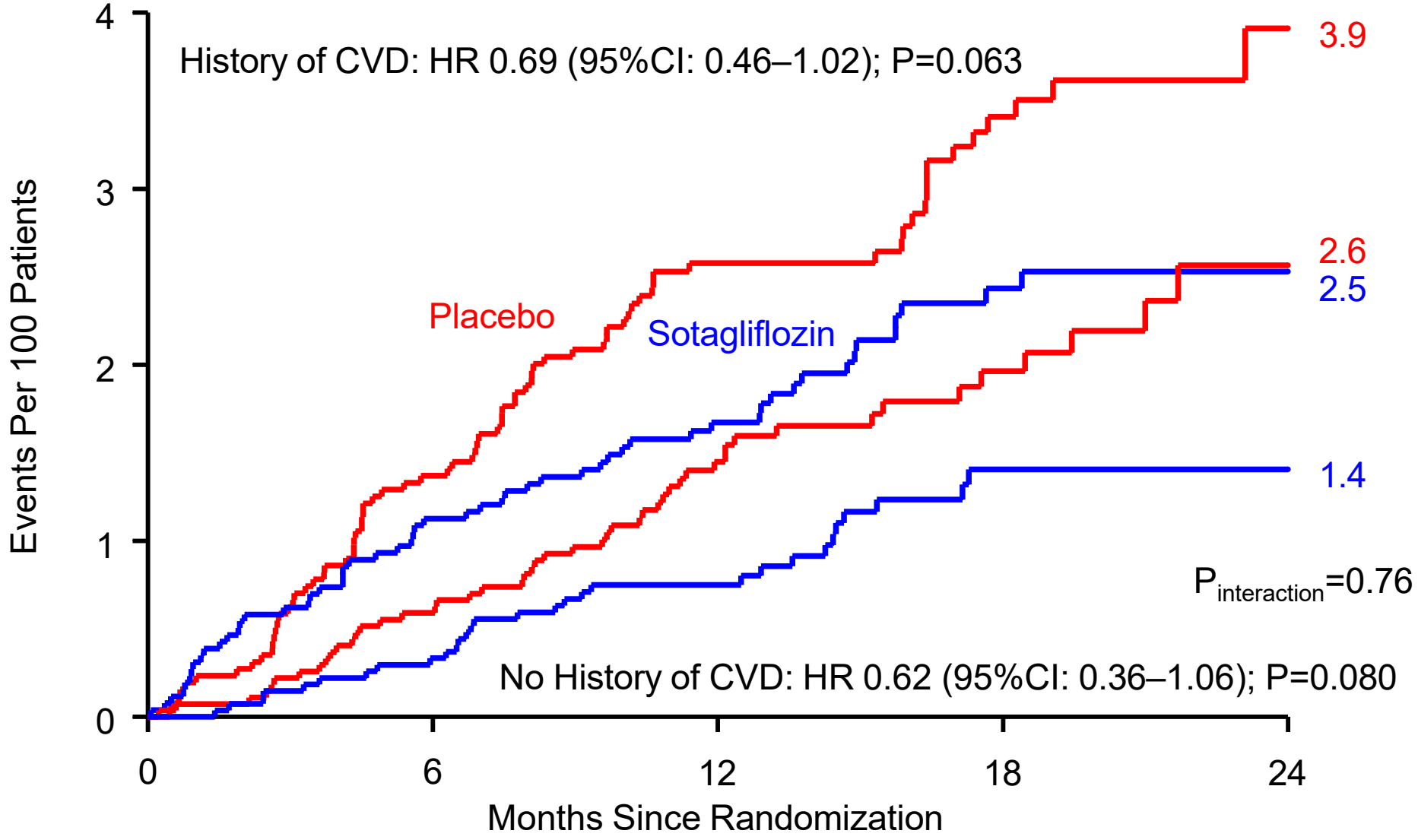
Bhatt DL, ACC 2022.

Total Stroke by CVD Subgroup



Bhatt DL, ACC 2022.

Total Stroke by CVD Subgroup

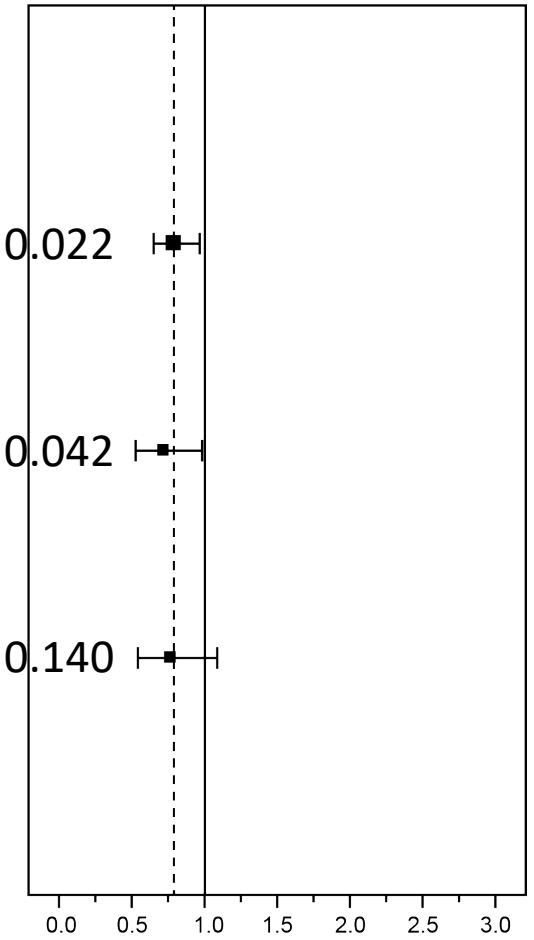


Bhatt DL, ACC 2022.

Consistent Benefit on MACE Across Vascular Beds

Subgroup	N	Events Per 100 py: Sotagliflozin	Events Per 100 py: Placebo	HR (95%CI)	P-value
Coronary Artery Disease	4943	6.13	7.77	0.79 (0.65, 0.97)	0.022
Cerebrovascular Disease	1777	7.03	9.54	0.72 (0.53, 0.99)	0.042
Peripheral Artery Disease	1393	6.76	9.50	0.77 (0.54, 1.09)	0.140

$P_{interaction}$=NS for all comparisons



Bhatt DL, ACC 2022.

Conclusions:

In patients with diabetes and chronic kidney disease, **sotagliflozin** significantly reduced the composite of total CV deaths, hospitalizations for HF, and urgent HF visits by **26%**

- With a very early benefit that was **significant by ~3 months**

Total CV deaths, MIs, and strokes were reduced by **23%,** potentially due to the SGLT1 effect of **sotagliflozin on MI and also stroke; this effect was significant by ~ 3 months**

MACE benefits were consistent across subgroups, including:

- **Prior coronary, cerebral, or peripheral artery disease**
- **And even without established cardiovascular disease**