

Prior HF Hospitalization, Clinical Outcomes, and Response to Sacubitril/Valsartan Compared with Valsartan in HFpEF



*Featured Science Presentation
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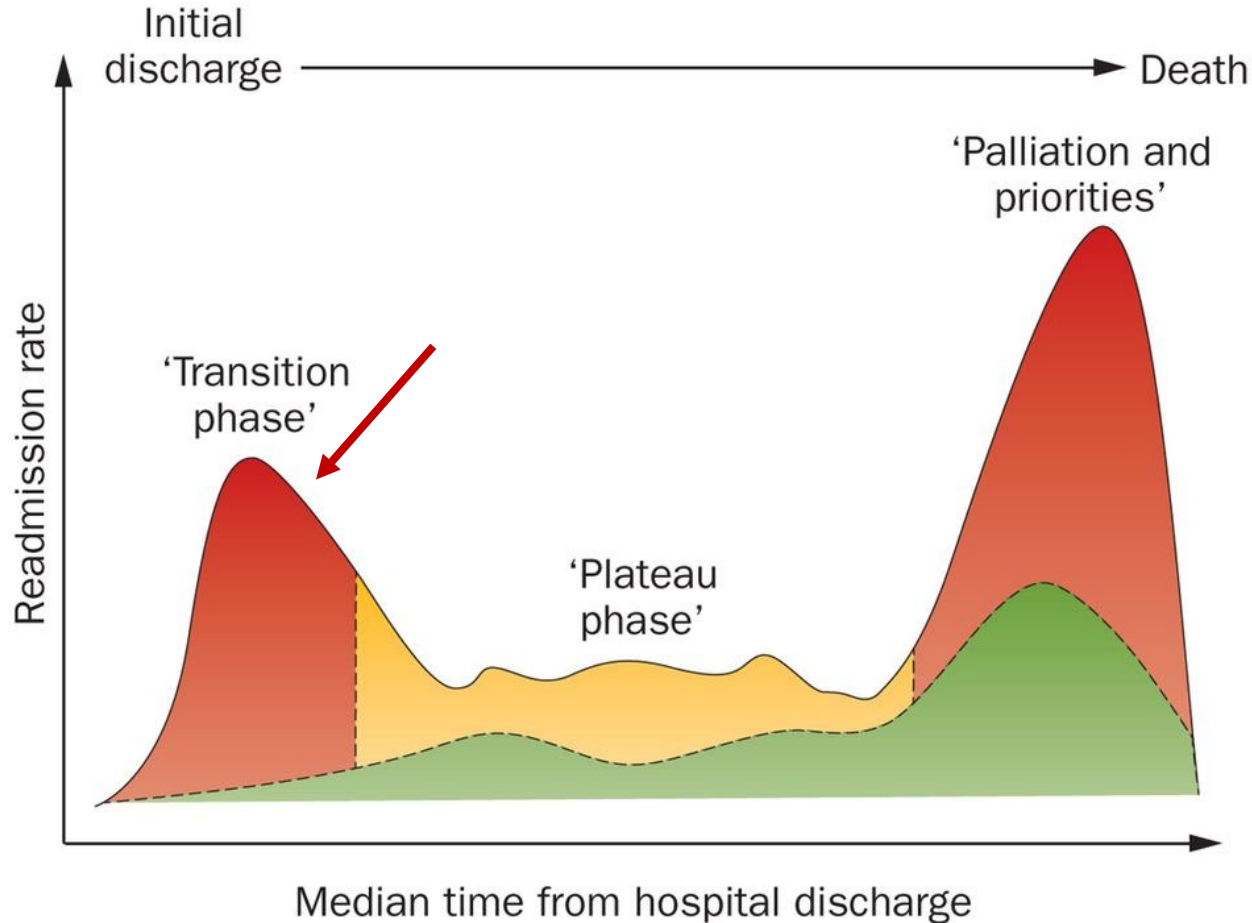
on behalf of the PARAGON-HF Investigators & Committees



Disclosures

- **Research Support:** NIH/NCATS KL2/Catalyst Medical Research Investigator Training award
- **Advisory Boards and/or Research Support:** Amgen, AstraZeneca, Baxter Healthcare, Bayer AG, Boehringer Ingelheim, & Relypsa
- **Clinical Endpoint Committee Member of PARAGON-HF**

High Risk Window after Hospital Discharge



PARAGON-HF: Sacubitril/Valsartan in HFpEF

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

MULTICENTER, DOUBLE-BLIND, ACTIVE-COMPARATOR TRIAL (PARAGON-HF)

4822

Patients with
NYHA class II–IV
heart failure and EF \geq 45%



Sacubitril–valsartan



97 mg + 103 mg
(twice daily)

(N=2419)

Valsartan

160 mg
(twice daily)



(N=2403)

**Total hospitalizations
for heart failure and
cardiovascular death**

894 events

1009 events

Rate ratio, 0.87; 95% CI, 0.75–1.01; P=0.06

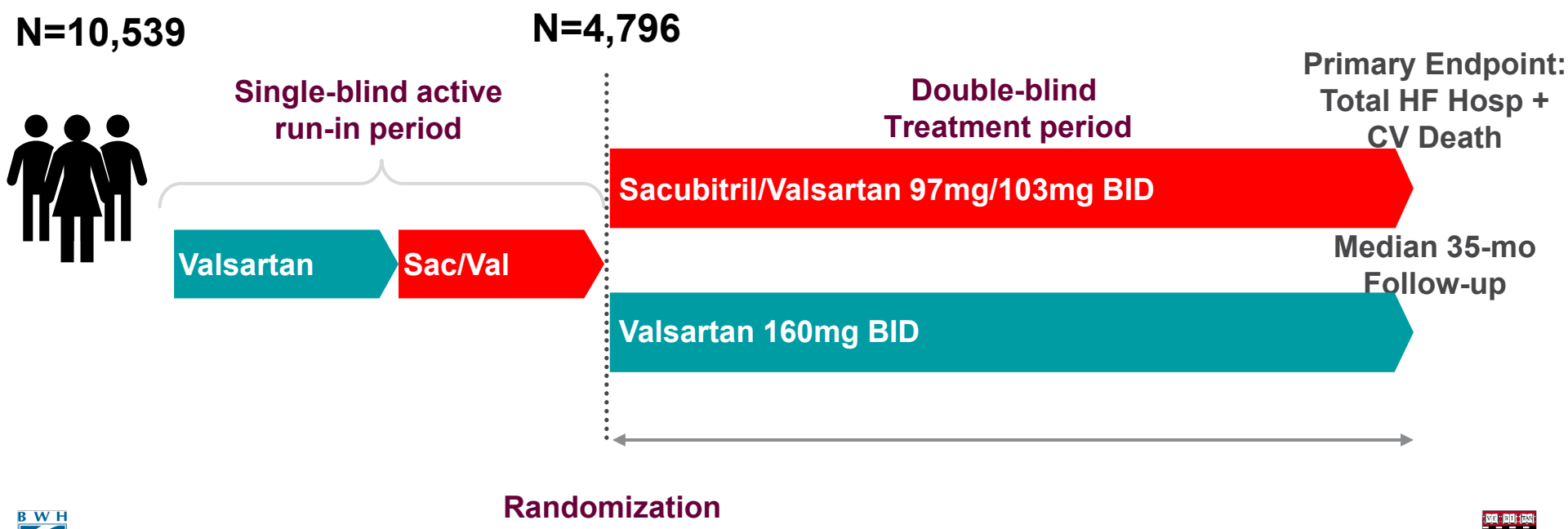
Objective

To determine whether the risk of clinical events and response to sacubitril/valsartan in HFpEF varies in relation to the proximity to HF hospitalization

PARAGON-HF: Study Design

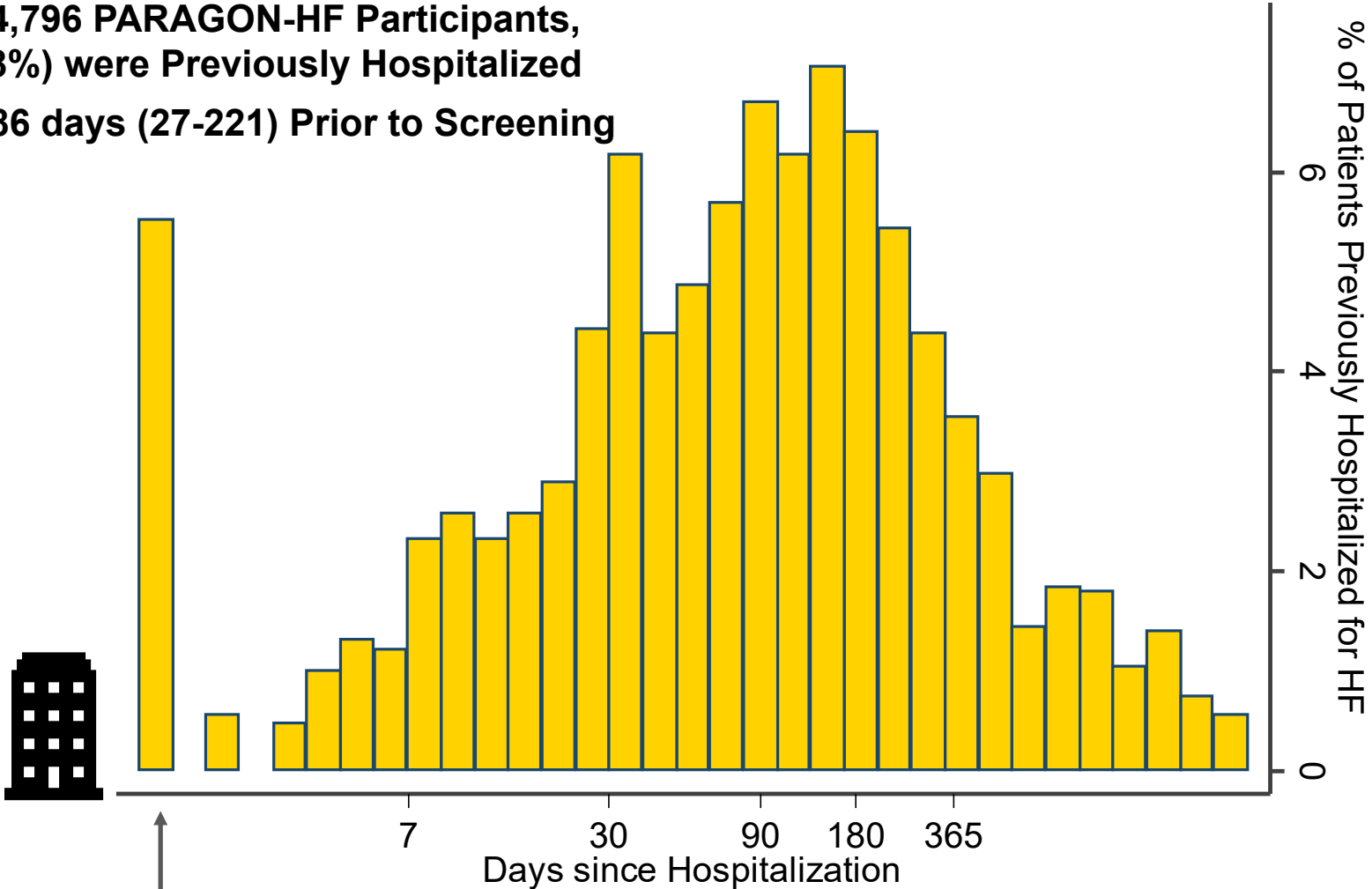


- Eligibility Criteria**
- Age ≥ 50 years
 - EF $\geq 45\%$
 - Elevated Natriuretic Peptides
 - Structural Heart Disease
 - Diuretic Therapy



Timing of Prior HF Hospitalization

Among 4,796 PARAGON-HF Participants,
2,306 (48%) were Previously Hospitalized
Median 86 days (27-221) Prior to Screening

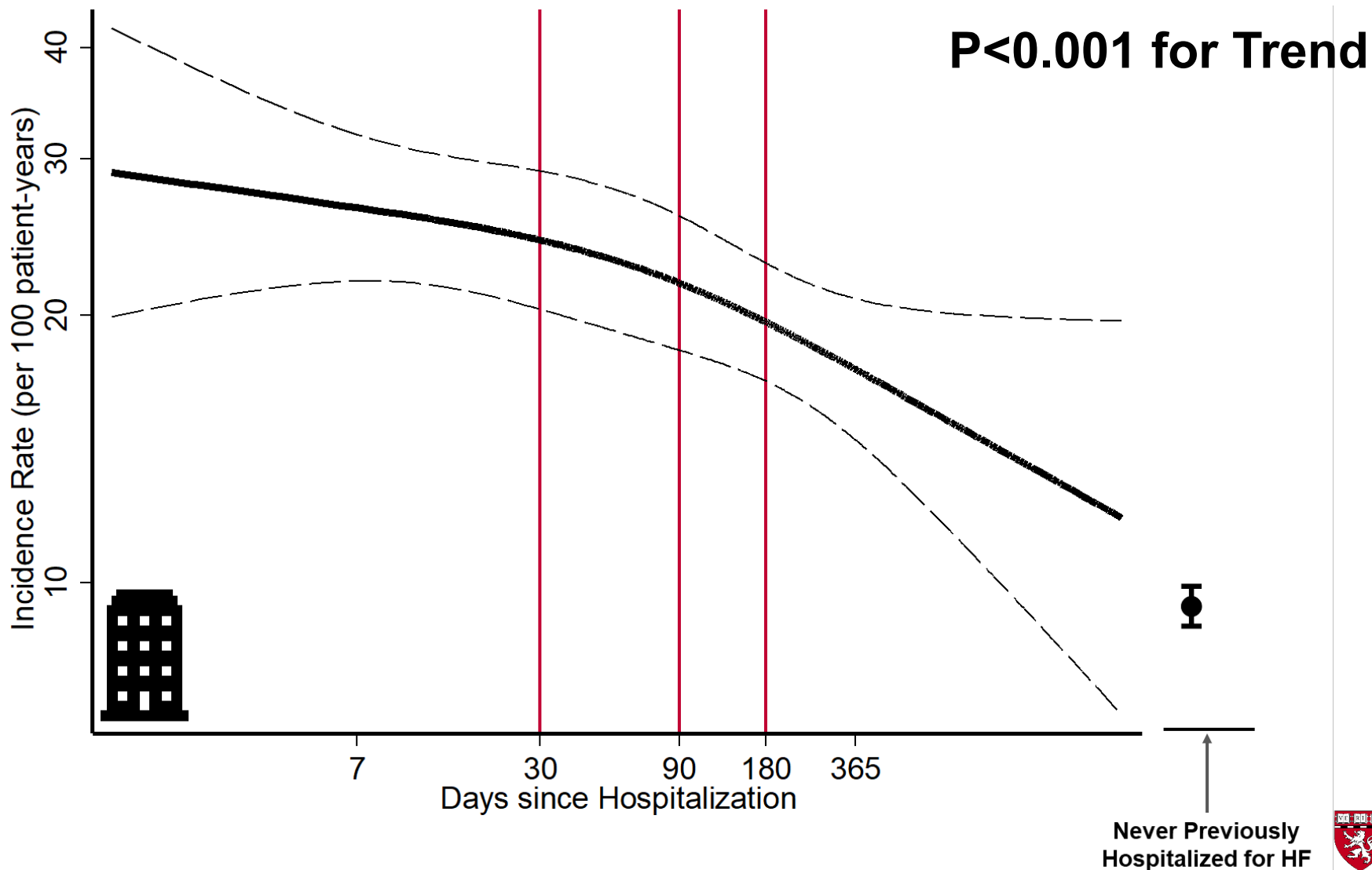


Baseline Characteristics

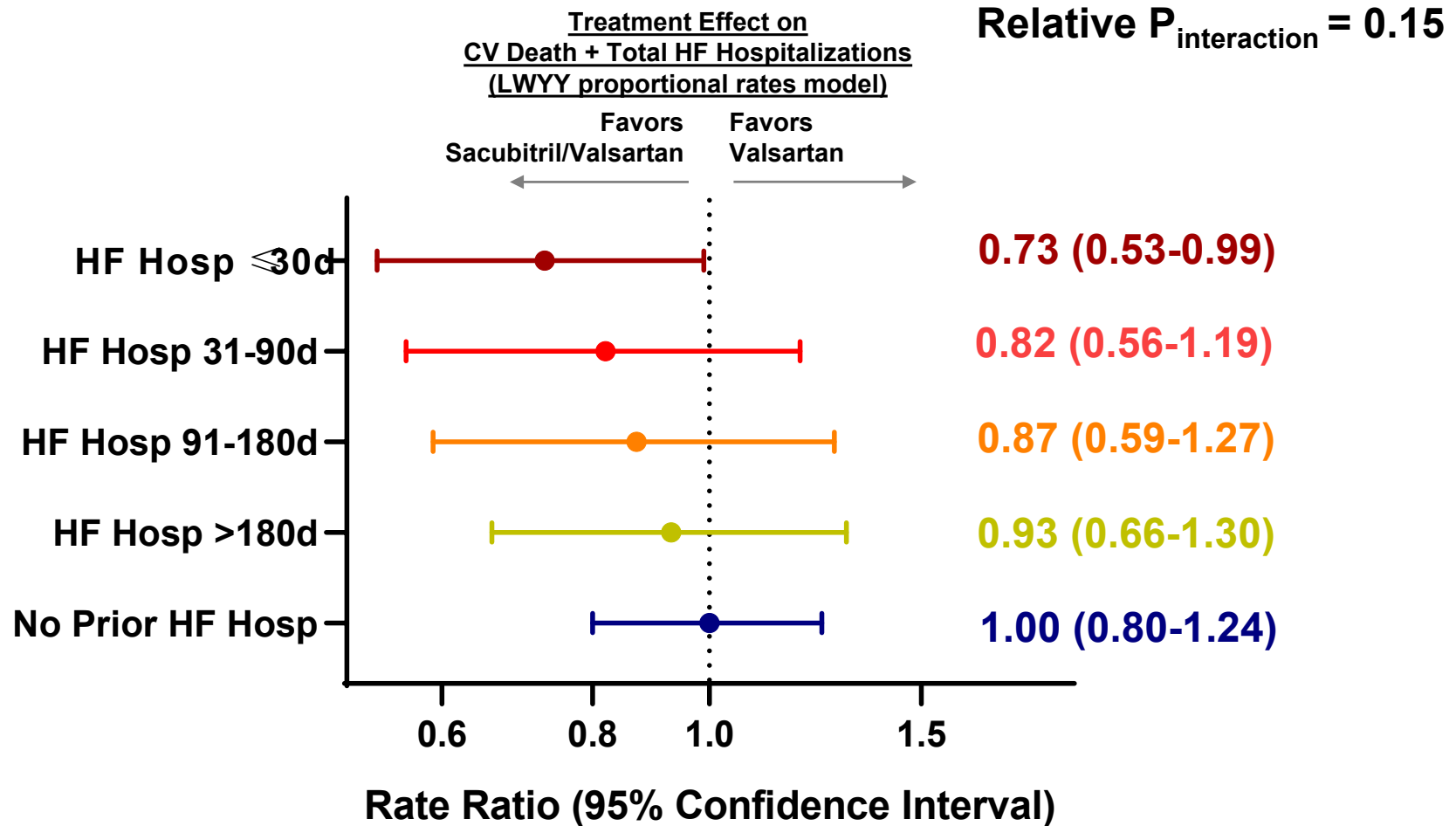
Time from Last Hospitalization for HF to Screening

	≤30 days (n=622)	31-90 days (n=555)	91-180 days (n=435)	>180 days (n=694)	No Prior HF Hosp (n=2,490)	P for trend
Sac/Val (%)	50%	51%	50%	47%	51%	0.56
Age (yrs)	72 ± 9	72 ± 9	72 ± 9	72 ± 9	73.5 ± 8	<0.001
Women (%)	54%	51%	47%	42%	55%	0.15
NT-proBNP	891 [425-1784]	843 [388-1779]	836 [381-1597]	948 [478-1717.5]	930 [489-1529.5]	0.16
Serum Cr (mg/dL)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	1.2 ± 0.3	1.1 ± 0.3	<0.001
SBP (mmHg)	131 ± 15	130.5 ± 16	132 ± 16	130 ± 16	130 ± 15	0.32
LVEF (%)	57 ± 8	58 ± 8	56.9 ± 8	56.9 ± 8	58 ± 8	0.006
AF/AFL	37%	34%	33%	34%	30%	<0.001

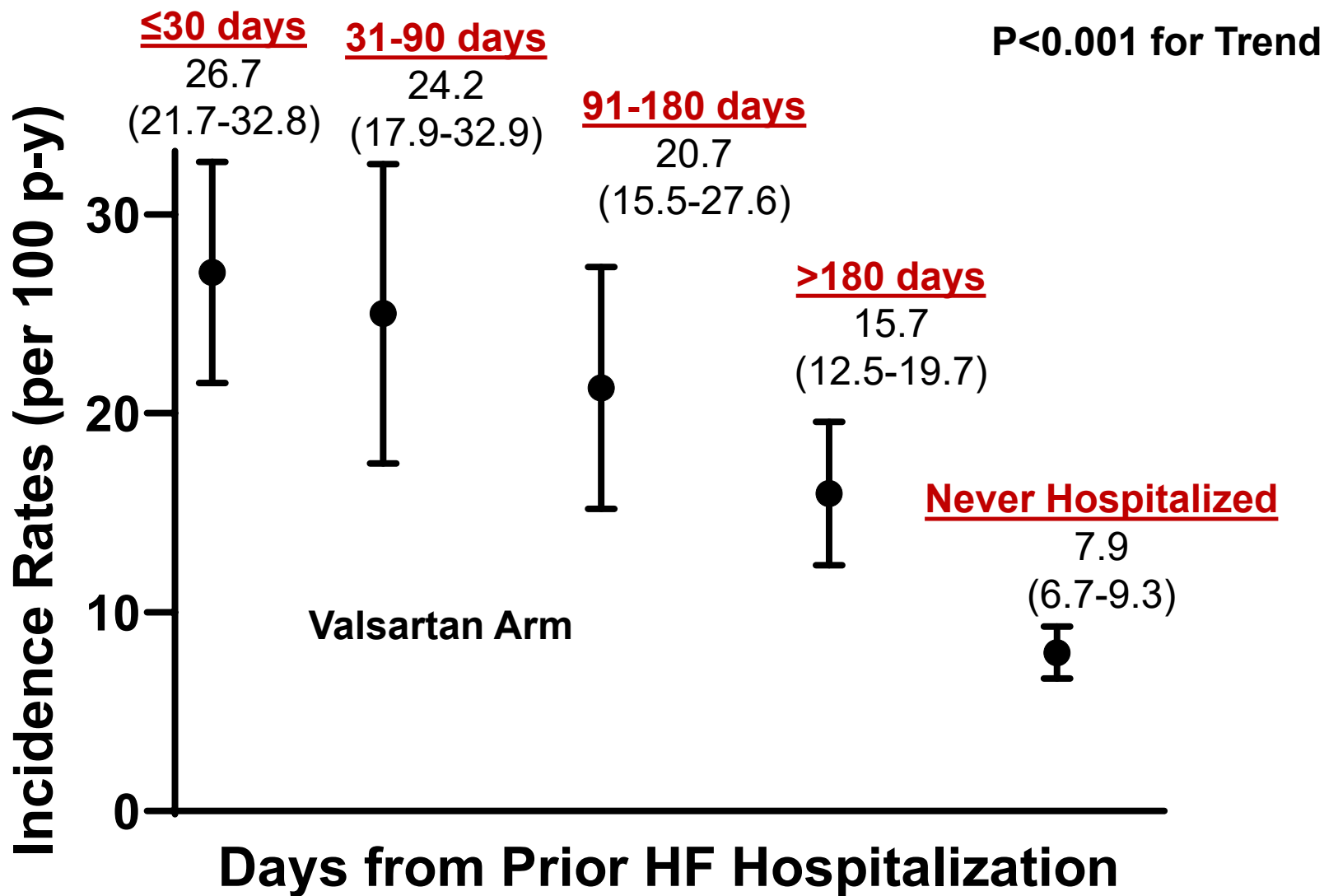
Risk Inversely & Non-Linearly Associated with Timing from Prior HHF



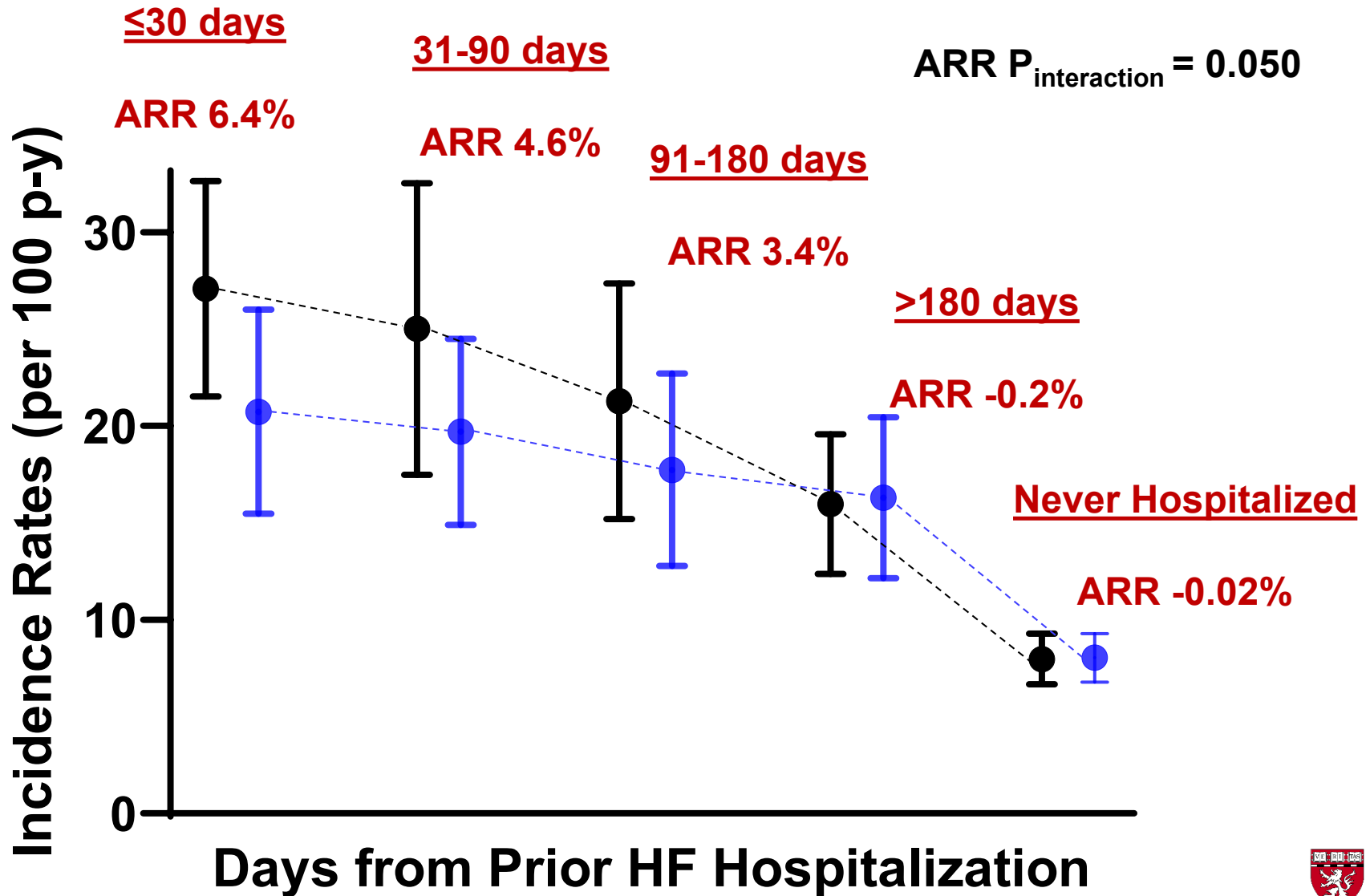
Gradient in Relative Risk Reduction



Higher Absolute Risk Reduction Among Patients Recently Hospitalized for HF



Higher Absolute Risk Reduction Among Patients Recently Hospitalized for HF



Summary: Sacubitril/Valsartan Early After Hospitalization for HFpEF

Patients with HFpEF who were recently hospitalized

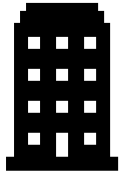


Face 2-3-fold higher risks of rehospitalization and CV death



Derive greater relative and absolute risk reductions with sacubitril/valsartan

Summary: Sacubitril/Valsartan Early After Hospitalization for HFpEF



Given intrinsic challenges with diagnosing HFpEF in ambulatory care, requirement of HF hospitalization may add certainty to the diagnosis



These hypothesis-generating data suggest that sacubitril/valsartan may safely blunt excess risk conferred in the high-risk post-discharge period and provide a rationale for further trials that assess sacubitril/valsartan in recently hospitalized HFpEF patients.

Simultaneous Publication in *JACC*



JACC

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

ORIGINAL INVESTIGATIONS

Just Accepted

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Drug Discontinuation Due to Serious Adverse Event

