



# Galectin-3 and Cardiovascular and Kidney Outcomes

## Individual Patient Data Meta-Analysis of 74,358 Patients from 5 Multinational Clinical Trials

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### BACKGROUND

- Galectin-3 (Gal-3) is a circulating biomarker linked to fibrosis of the heart and kidneys.
- It has been suggested to be causally related to heart failure (HF), although its prognostic role for cardiovascular diseases and kidney outcomes remains unclear.
- An **individual patient data meta-analysis** of **five multinational clinical trials** (DECLARE, FOURIER, PEACE, REVEAL, SOLID) enrolling patients at high risk for or with established vascular disease was conducted.
- Gal-3** (Abbott Diagnostics) had been measured in the TIMI Clinical Trials Lab using baseline samples
- Outcomes** analyzed were CV death (CVD), hospitalization for HF (HHF), and a kidney composite endpoint (Kidney-EP in FOURIER and DECLARE only:  $\geq 40\%$  decrease in eGFR to  $< 60$  mL/min, end-stage kidney disease, or renal death).
- Cox models were adjusted for patient characteristics, CV risk factors, NTproBNP, hs-cTnI or T, hs-CRP, and baseline eGFR.

### RESULTS

- Overall, **74,358 patients were included**.
- Baseline characteristics by Gal-3 are shown in **Table 1**.
- Gal-3 was weakly correlated with eGFR, NTproBNP, hs-CRP, hs-cTnI, and hs-cTnT (all  $p < 0.001$ ; **Table 2**).
- Higher baseline Gal-3 was associated with significantly higher 3y event rates for all endpoints (**Figure 1**).
- Upon adjustment, Gal-3 was significantly associated with a higher risk for CVD analyzed either by quartile (**Figure 2**) or continuously per 1-SD (adj-HR per 1-SD 1.16 [1.1-1.21],  $p < 0.001$ ), HHF (1.16 [1.11-1.22],  $p < 0.001$ ) and the Kidney-EP (1.27 [1.2-1.36],  $p < 0.001$ ).
- Results were consistent among patients with prior HF or established CKD (**Figure 3 & 4**).

Table 1: Baseline characteristics

Galectin-3 quartiles	Q1 (N=18,305)	Q2 (N=18,424)	Q3 (N=19,006)	Q4 (N=18,623)
Range in ng/L	$< 12.9$ ng/L	12.9- $< 15.7$	15.7-19.3	$\geq 19.3$
Age	62 (56-67)	63 (58-69)	65 (60-71)	67 (62-74)
Male sex	84.1	80.2	74.8	66.7
Body mass index (kg/m <sup>2</sup> )	29 (26-32)	29 (26-32)	29 (26-32)	29 (26-33)
Hypertension	79.1	78.2	79.2	83.7
Diabetes	46.6	43.9	46.6	51.8
CAD	72.5	75.1	75.2	73.2
Prior heart failure	12.6	12.5	12.7	16.2
Atrial fibrillation	6.3	7.1	8.5	11.0
eGFR	91 (80-99)	87 (75-96)	83 (69-93)	72 (57-87)
$< 60$ mL/min	3.3	6.0	11.3	29.2

% or median (25<sup>th</sup>-75<sup>th</sup> percentile)

Table 2: Correlation of galectin-3 with other biomarkers

Galectin-3	eGFR	NTproBNP	hs-CRP	hs-cTnI	hs-cTnT
all $p < 0.001$	$r = -0.36$	$r = 0.22$	$r = 0.11$	$r = 0.16$	$r = 0.21$

FIGURE 1: 3-year KM event rates

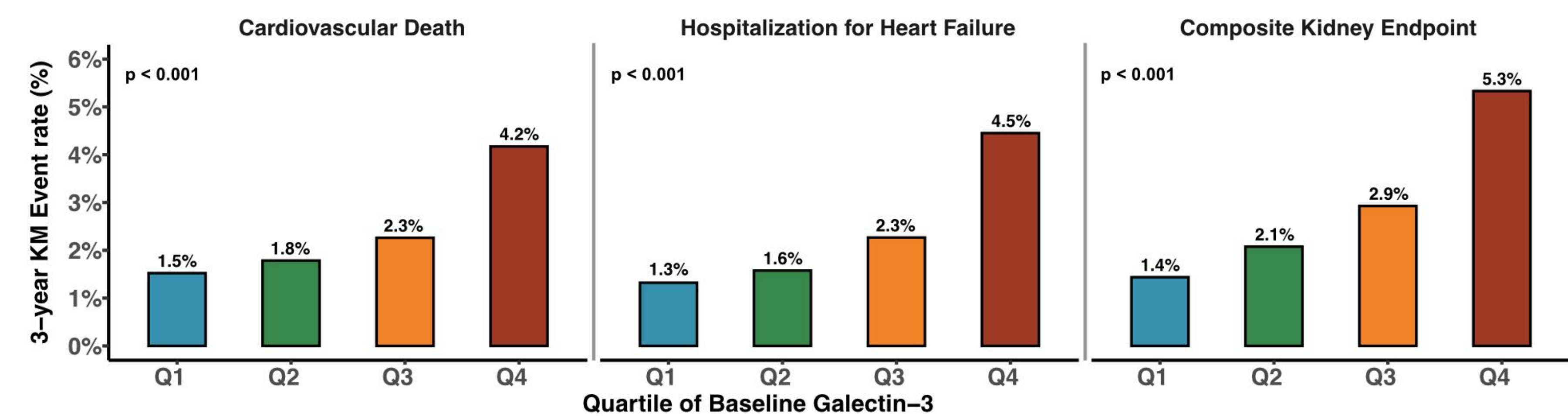


FIGURE 2: adj. HR per quartiles of galectin-3

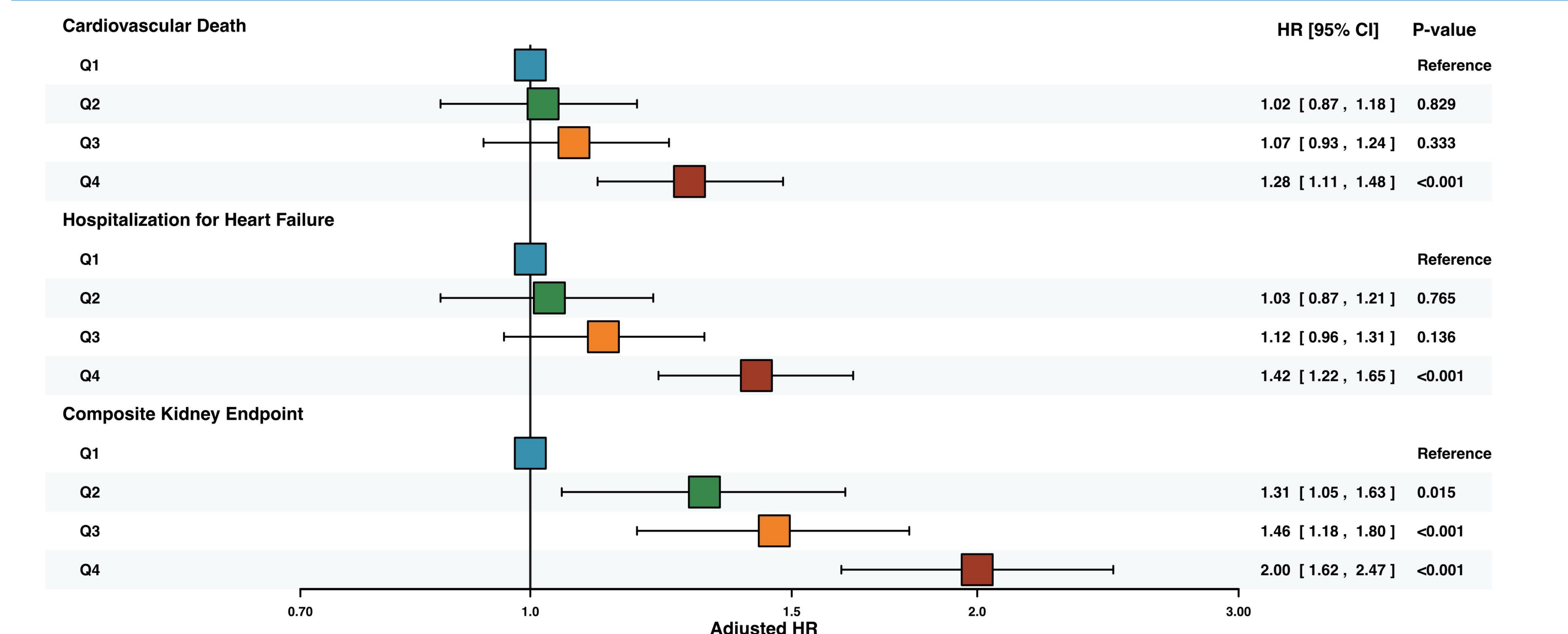


FIGURE 3: 3-year KM rates in sub-groups of heart failure (A) and CKD (B)

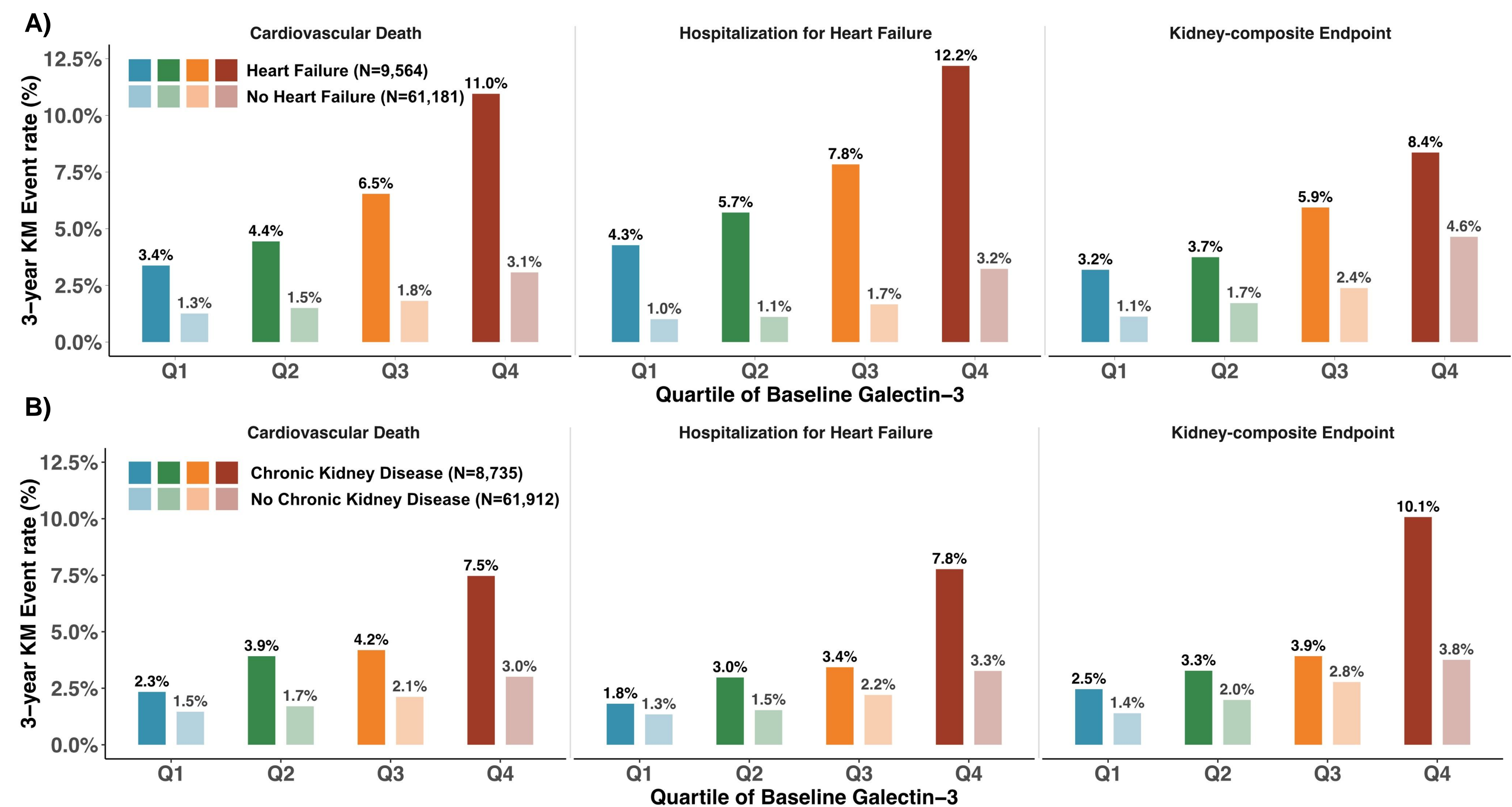
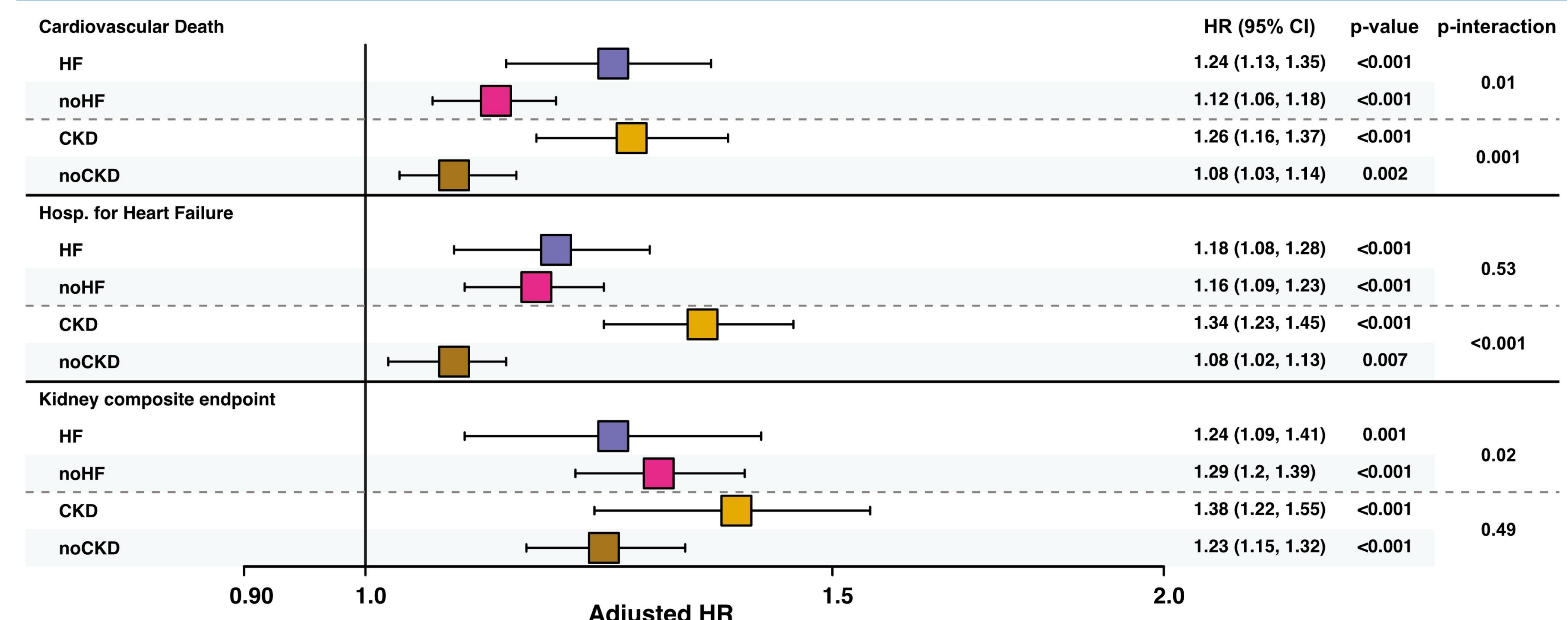


FIGURE 4: Adjusted hazard ratio of galectin-3 per 1-SD in sub-groups



### CONCLUSION

- Plasma **Gal-3 is independently associated with future HF events and decline in kidney function** beyond traditional risk factors and biomarkers & within important subgroups.
- Gal-3 remains a promising biomarker of organ fibrosis that is prognostic across a spectrum of pts at risk for or with established CV disease.



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