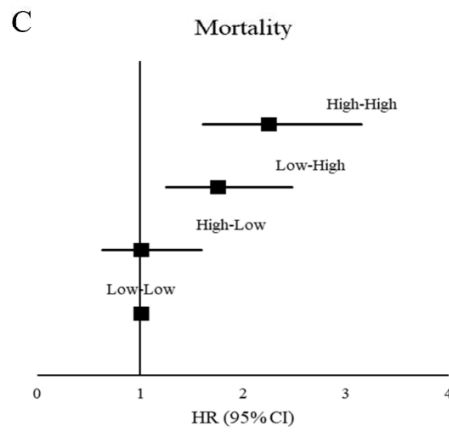
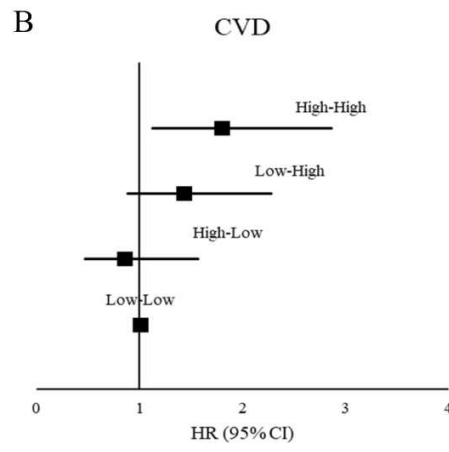
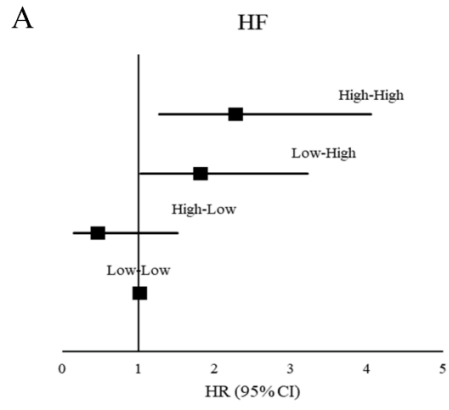


**Online Figure 1.** Hazard ratios and 95% confidence intervals of HF, CVD, and mortality for classes of longitudinal change in galectin-3

Persistently high levels of Gal-3 were associated with significantly higher risk of incident HF (A), incident CVD (B), and all-cause mortality (C). High-high, low-high, high-low, and low-low represent classes of change in Gal-3 between the earlier exam and the later exam using the clinical cut-off of 17.8 ng/ml. CVD = cardiovascular disease, HF = heart failure, HR (95% CI) = hazard ratio (95% confidence interval).



**Online Table 1.** Association between change in galectin-3 and incident outcomes not adjusting for baseline galectin-3 levels

Outcome/Model	Change in Gal-3	
	HR (95% CI)	P-value
<b>Incident heart failure</b>		
Age, sex- adjusted	1.55 (1.28-1.88)	<0.0001
Multivariable- adjusted*	1.31 (1.07-1.61)	0.0098
<b>Incident cardiovascular disease</b>		
Age, sex- adjusted	1.34 (1.17-1.55)	<0.0001
Multivariable- adjusted*	1.23 (1.06-1.43)	0.0066
<b>Mortality</b>		
Age, sex- adjusted	1.33 (1.20-1.48)	<0.0001
Multivariable- adjusted*	1.20 (1.08-1.35)	0.0012

\*Multivariable models are adjusted for age, sex, systolic blood pressure, antihypertensive treatment, diabetes, body mass index, smoking, left ventricular hypertrophy, high-density lipoprotein (HDL) to cholesterol ratio, estimated glomerular filtration rate, prevalent cardiovascular disease (except for CVD model). Mortality was further adjusted for prevalent heart failure.

†Hazard ratio and 95% confidence intervals for 1 standard deviation

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(SD) increase in log-Gal3 levels over a 10-year period. This corresponds to 3.3 ng/ml change in Gal-3.

**Online Table 2.** Association between longitudinal change in galectin-3 and incident outcomes after further adjusting for baseline BNP

Outcome/Model (Events/At risk)	HR (95% CI) †	P-value
Incident heart failure (108/2417)		
Age, sex, baseline Gal-3- adjusted	1.55 (1.29 - 1.87)	<0.0001
Multivariable- adjusted*	1.35 (1.10 - 1.67)	0.004
Incident cardiovascular disease (213/2268)		
Age, sex, baseline Gal-3- adjusted	1.39 (1.21 - 1.60)	<0.0001
Multivariable- adjusted*	1.28 (1.10 - 1.49)	0.001
Mortality (342/2456)		
Age, sex, baseline Gal-3- adjusted	1.34 (1.21 - 1.48)	<0.0001
Multivariable- adjusted*	1.29 (1.15 - 1.44)	<0.0001

\*Multivariable models are adjusted for baseline galectin-3 levels, age, sex, systolic blood pressure, antihypertensive treatment, diabetes, body mass index, smoking, left ventricular hypertrophy, high-density lipoprotein (HDL) to cholesterol ratio, estimated glomerular filtration rate, prevalent cardiovascular disease (except for CVD model) as well as brain natriuretic peptide (BNP). Mortality was further adjusted for prevalent heart failure.

†Hazard ratio and 95% confidence intervals for 1 standard deviation (SD) increase in log-Gal3 levels over a 10-year period. This corresponds to 3.3 ng/ml change in Gal-3.

**Online Table 3.** Association between quartiles of longitudinal change in galectin-3 and clinical outcomes

Quartile	Heart failure (108 events)		Cardiovascular disease (213 events)		Mortality (348 events)	
	HR (95% CI)*	P-value	HR (95% CI)*	P-value	HR (95% CI)*	P-value
	Referent		Referent		Referent	
Quartile 2	1.23 (0.61-2.50)	0.56	1.29 (0.83-2.01)	0.25	1.02 (0.70-1.47)	0.92
Quartile 3	1.49 (0.75-2.93)	0.25	1.23 (0.79-1.91)	0.37	1.19 (0.84-1.70)	0.33
Quartile 4	1.91 (0.97-3.76)	0.06	1.74 (1.12-2.71)	0.01	1.94 (1.37-2.73)	0.0002
P for trend		0.04		0.02		<0.0001

\*HR (95%CI) represents hazard ratio (95% confidence interval) using a multivariable-adjusted model adjusting for baseline galectin-3 levels, age, sex, systolic blood pressure, antihypertensive treatment, diabetes, body mass index, smoking, left ventricular hypertrophy, high-density lipoprotein (HDL) to cholesterol ratio, estimated glomerular filtration rate, prevalent cardiovascular disease (except for CVD model). Mortality was further adjusted for prevalent heart failure.

**Online Table 4.** Association between classes of longitudinal change in galectin-3 and clinical outcomes

	Heart failure		Cardiovascular disease		Mortality	
	HR (95% CI)*	P-value	HR (95% CI)*	P-value	HR (95% CI)*	P-value
High-High	2.28 (1.28-4.05)	0.0005	1.80 (1.13-2.86)	0.01	2.25 (1.61-3.15)	<0.0001
Low -High	1.82 (1.03-3.22)	0.04	1.43 (0.89-2.28)	0.13	1.76 (1.25-2.48)	0.0012
High-Low	0.47 (0.15-1.51)	0.20	0.86 (0.47-1.57)	0.62	1.01 (0.63-1.60)	0.97
Low-Low	Referent		Referent		Referent	

\*HR (95%CI) represents hazard ratio (95% confidence interval) for categories of trend as compared to reference level of low-low using a multivariable-adjusted model adjusting for baseline galectin-3 levels, age, sex, systolic blood pressure, antihypertensive treatment, diabetes, body mass index, smoking, left ventricular hypertrophy, high-density lipoprotein (HDL) to cholesterol ratio, estimated glomerular filtration rate, prevalent cardiovascular disease (except for CVD model). Mortality was further adjusted for prevalent heart failure.

High-high, low-high, high-low, and low-low represent classes of change in Gal-3 between the earlier exam and the later exam using the clinical cut-off of 17.8 ng/ml.