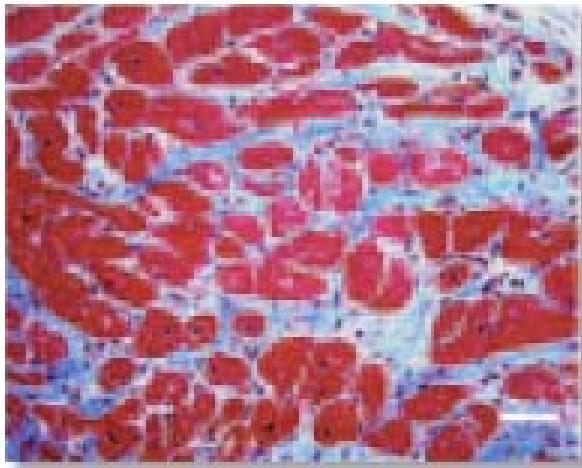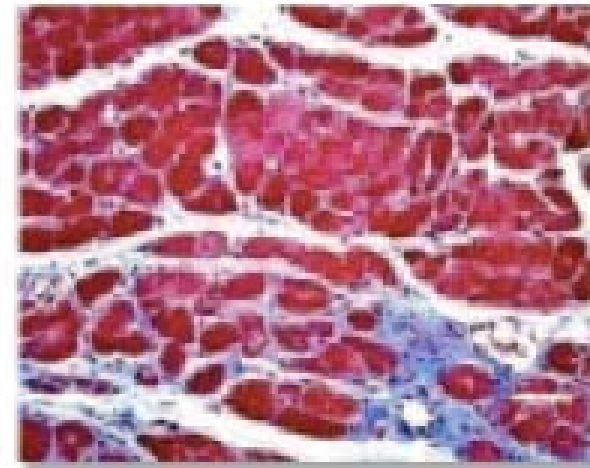# Long-term Predictive Value of Soluble ST2 Level and Left Ventricular Function: The EGAT Study.

Wisuit Katekao MD, Poh Chanyavanich MD, Somluck Ninwaranon MD,

Prin Vathesatogkit MD, Oraporn See MD,

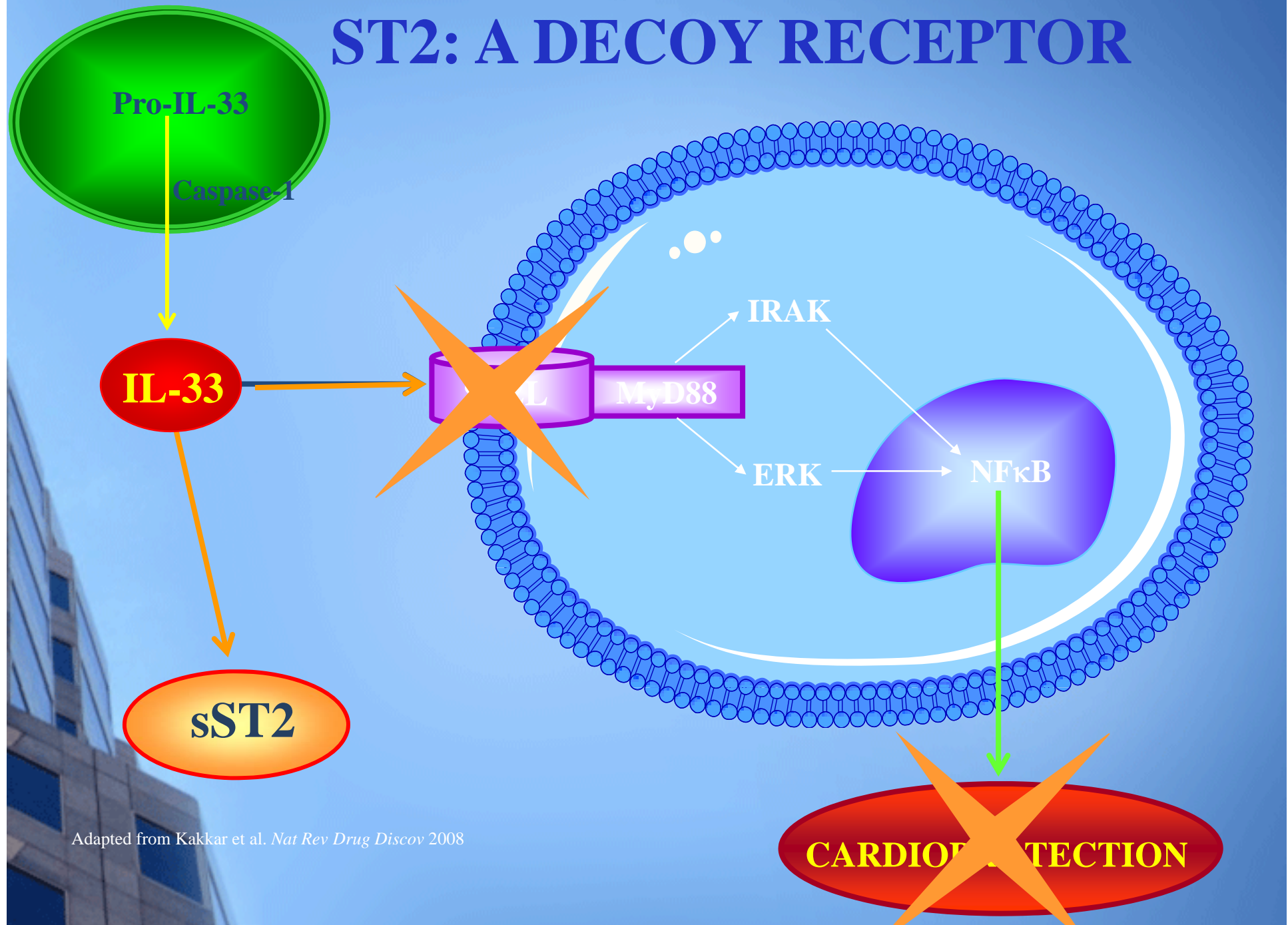Sukit Yamwong MD and Piyamitr Sritara MD

Novel IL-33 treatment

Control

IL-33 treated[3]

ST2: A DECOY RECEPTOR

Pro-IL-33

Caspase-1

IL-33

sST2

IRAK

MyD88

ERK

NFκB

CARDIOPROTECTION

sST2 = Decoy Receptor

- " It has been subsequently demonstrated that high levels of soluble ST2 can block IL-33's activity, thus preventing the cardioprotective effect. "

- High sST2 = More Fibrosis in myocardium

    = More Cardiovascular event

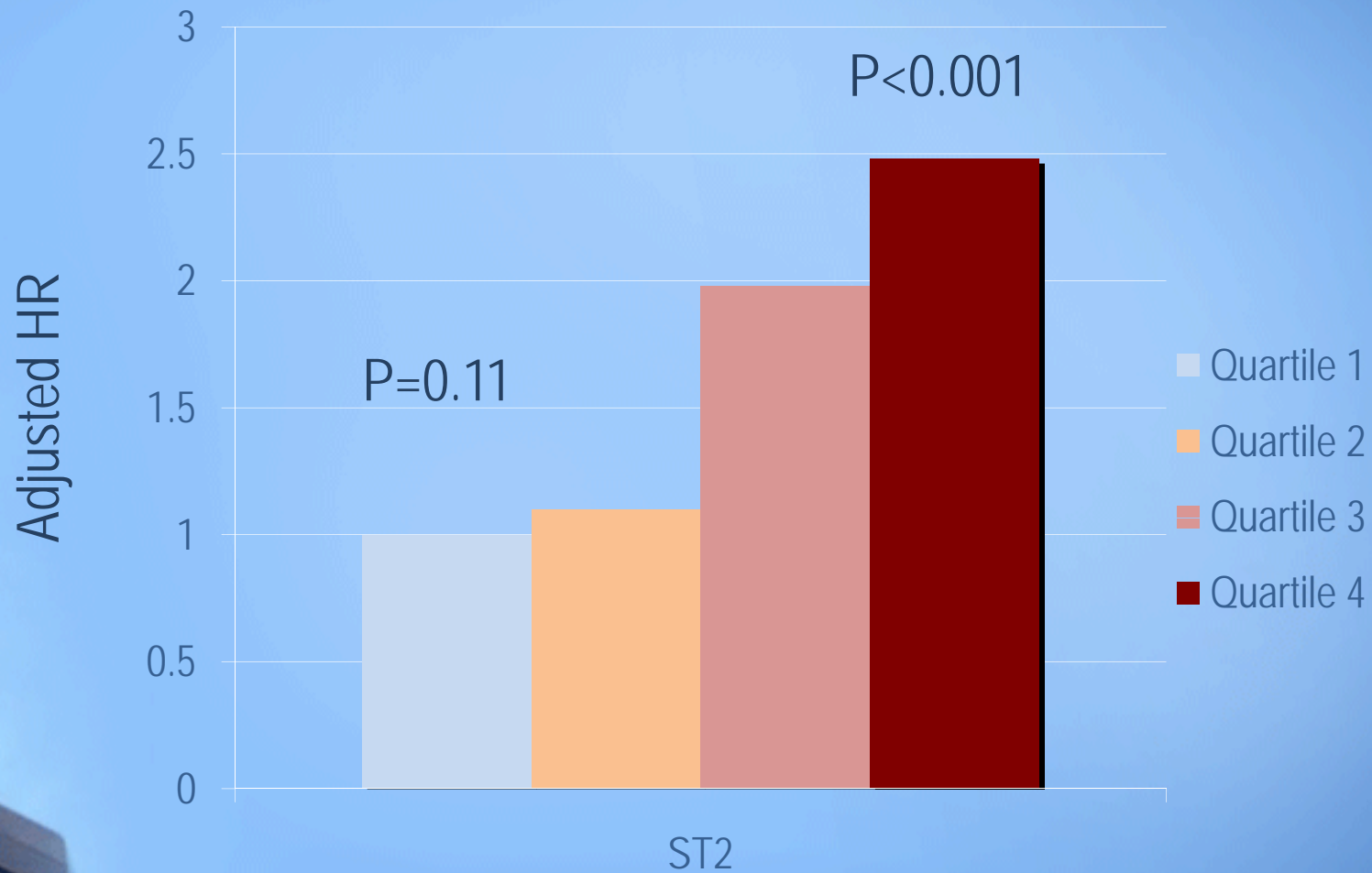   (including **new-onset heart failure** and mortality)

Abnormalities in ST2 lead to a phenotype of cardiac remodeling

Interruption of ST2 results in **increased LV mass, LVH, more dilated LV chambers, and worse LV function**

Seki, et al, Circ HF, 2009
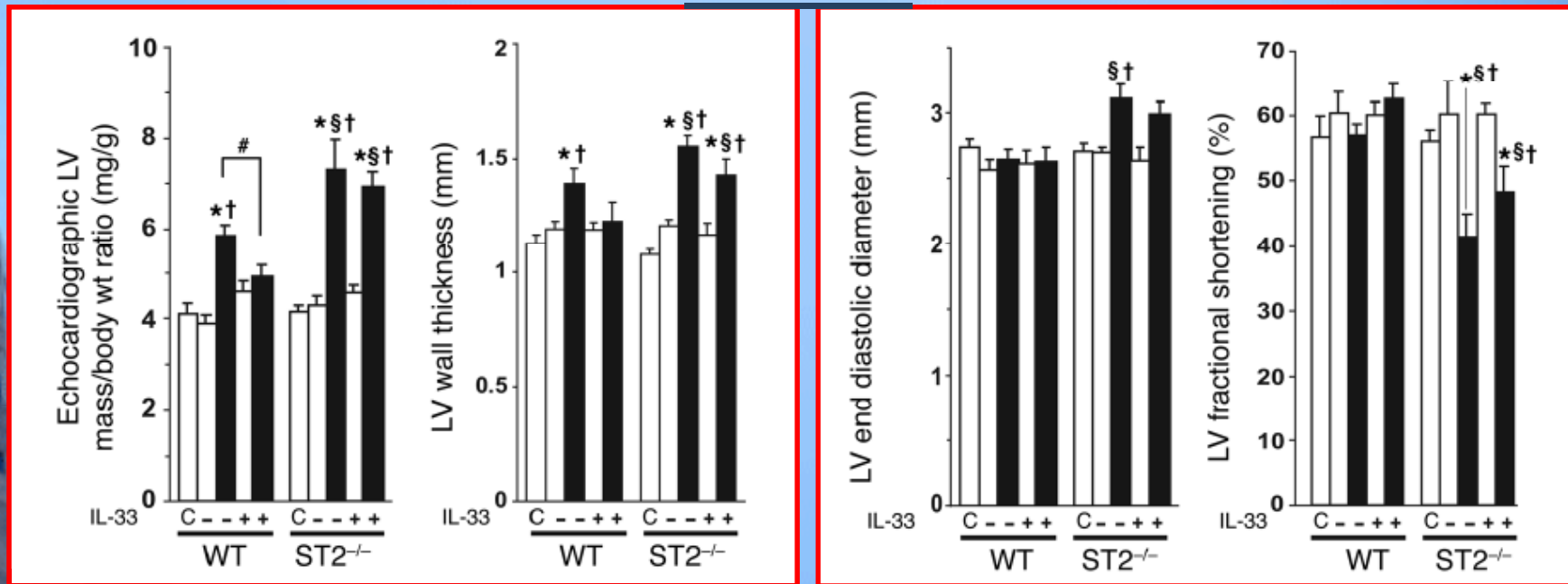
sST2 predicts **new-onset HF** in the community
The Framingham Heart Study

Wang TJ et al. Circulation. 2012;126:1596-1604

Background

- Hypertension is a well-known cause of diastolic dysfunction and cardiac remodeling.

- Soluble ST2 has proven to have a strong predictor for cardiovascular events, including mortality and new-onset heart failure.

Method

- We hypothesized that high level of sST2, similar to hypertension, have a power to predict cardiac remodeling, such as changes in size and function of the left ventricle before symptoms arise.

EGAT study in 2002

Baseline data
- Serum sST2 level
- Hypertension
- Other underlying diseases
- Physical examination
- Other laboratory values

10 years →

EGAT study in 2012

Echocardiographic indices
- Systolic function
- Diastolic function
- Chamber quantification

Soluble ST2

- We assess sST2 level by the Presage(®) ST2 Assay (Critical Diagnostics, CA, USA).

Reproducibility

- Case selection / Method of contouring / Practice
- Intraobserver
    - 20+ patients
    - 2 different time points (2-4 wks in random)
- Interobserver
    - 20+ patients

Soluble ST2 (ng/ml)

	This Study (Subset of EGAT study)	EGAT Study	Framingham Study
Mean $\pm$ SD	18.99 $\pm$ 8.65	19.8 $\pm$ 9.2	n/a
Percentile 25	**13.95** (M: 14.30) (F: 12.35)	14.7	**16.9** (M: 19.20) (F: 15.27)
Percentile 50	**17.40** (M: 18.10) (F: 15.10)	18.3	**21.0** (M: 23.58) (F: 18.77)
Percentile 75	**21.80** (M: 22.50) (F: 19.60)	22.9	**26.1** (M: 29.07) (F: 23.15)

Baseline Characteristics

Age, year		
Male, %		
sST2 level, ng/ml		
Hypertension, %		
DM, %		
SystolicBP		
MeanABP		
Weight, Kgs		
Creatinine, mg/dl		

Head-to-Head (4th quartile and HT)

	4th Quartiles sST2 (n = 143)	HT (n = 144)	*p*-value
Age, year	58.0 ± 4.4	58.9 ± 4.4	n/a
Male, %	81.1	79.8	n/a
sST2 level, ng/ml	**27.0** (23.6-30.9)	**17.3** (14.4-23.0)	n/a
Hypertension, %	**26.9**	**100.0**	n/a
DM, %	13.9	18.7	n/a
SystolicBP	124.2 ± 16.6	139.6 ± 17.6	n/a
MeanABP	94.3 ± 11.3	104.9 ± 11.6	n/a
Weight, Kgs	66.2 ± 13.0	67.6 ± 13.3	n/a
Creatinine, mg/dl	1.21 ± 0.28	1.20 ± 0.28	n/a

Result

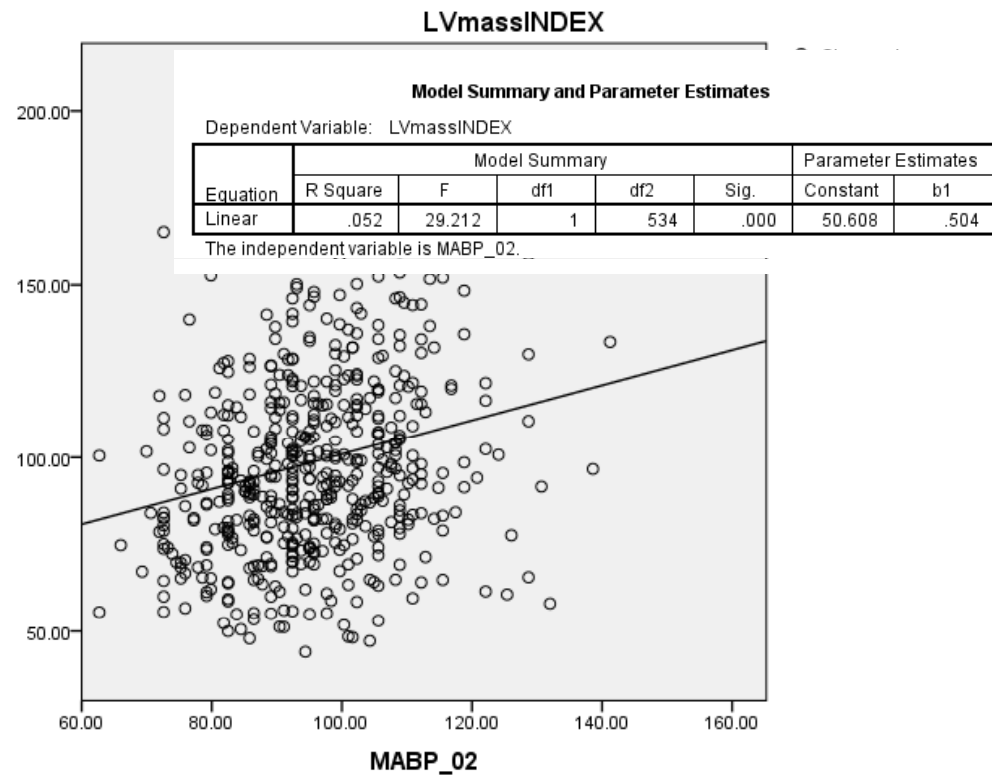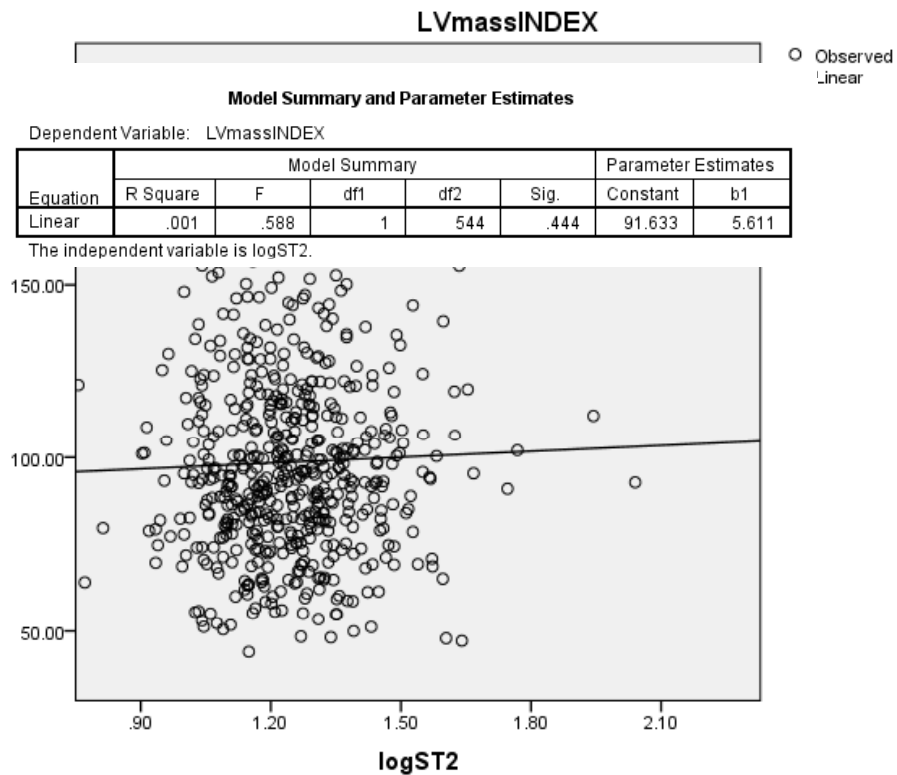|			
Mitral E, m/s			
Mitral E/A			
Lateral E′, m/s			
Lateral E/E′			
IVSd, mm			
PWd, mm			
LVEF, %			
LV mass index, g/m2			
RWT, mm			
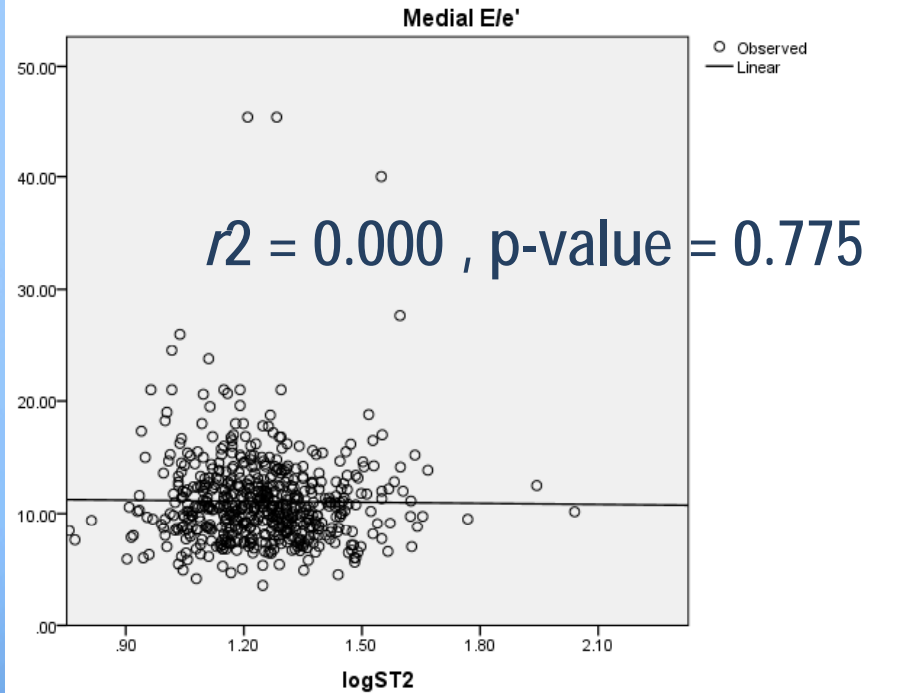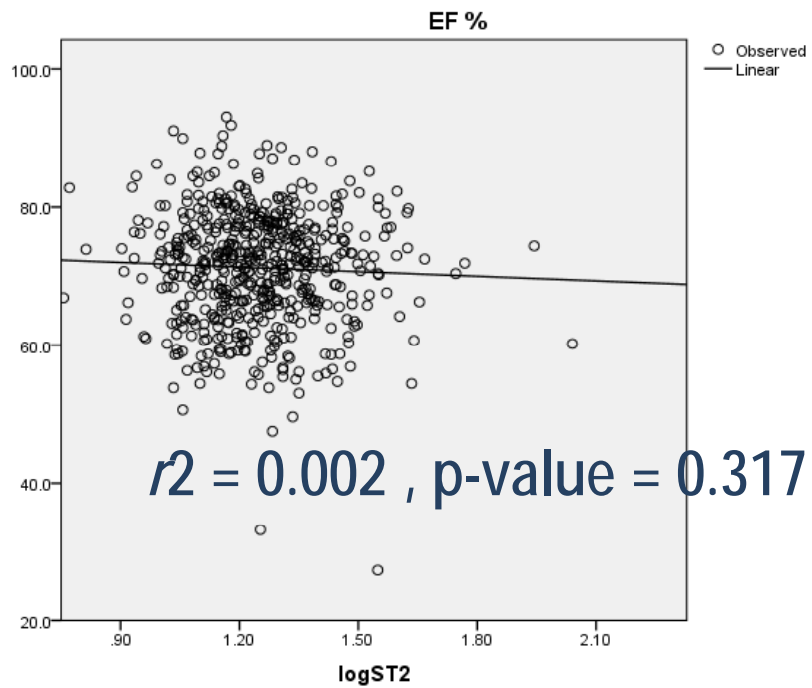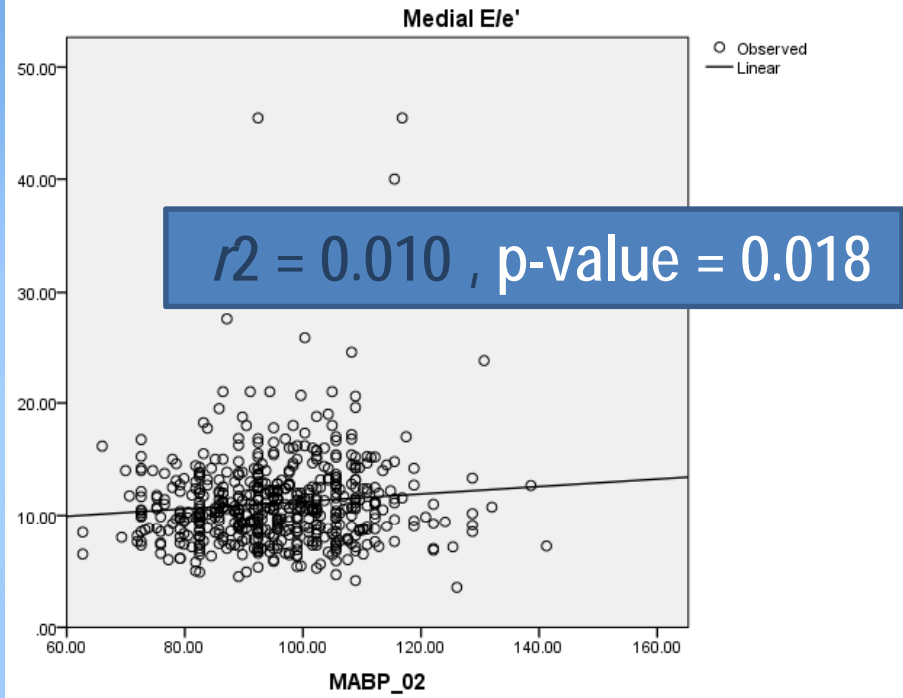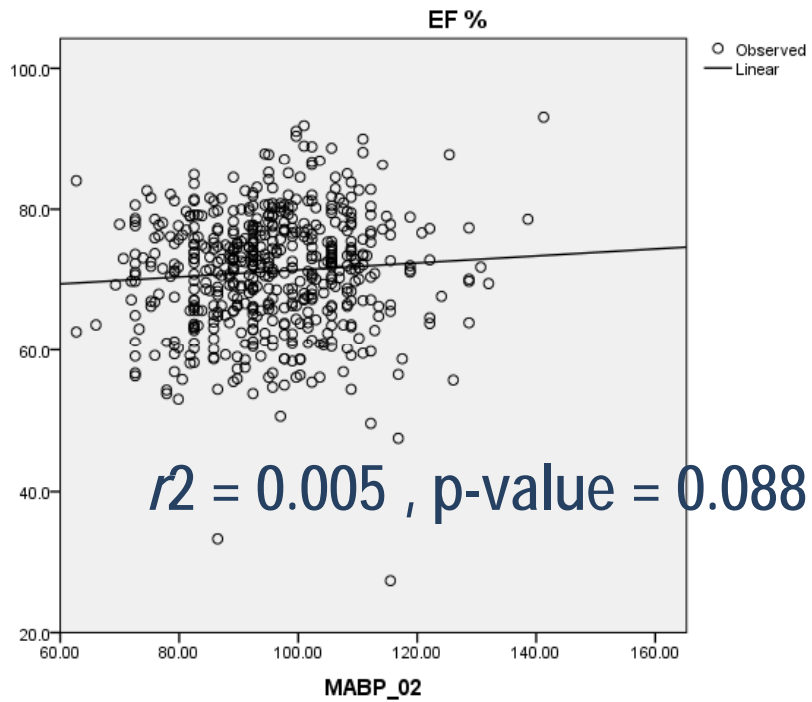
- **Mean arterial blood pressure** is a good predictor for left ventricular mass index, during 10 years follow-ups.

$r2 = 0.001$, p-value = 0.444

$r2 = 0.052$, p-value = 0.000

LVmassINDEX

Model Summary and Parameter Estimates

Dependent Variable: LVmassINDEX

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.001	.588	1	544	.444	91.633	5.611

The independent variable is logST2.

LVmassINDEX

Model Summary and Parameter Estimates

Dependent Variable: LVmassINDEX

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.052	29.212	1	534	.000	50.608	.504

The independent variable is MABP_02.

RWT

Model Summary and Parameter Estimates

Dependent Variable: RWT

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.012	6.262	1	534	.013	.374	.001

The independent variable is MABP_02.

p-value 0.013
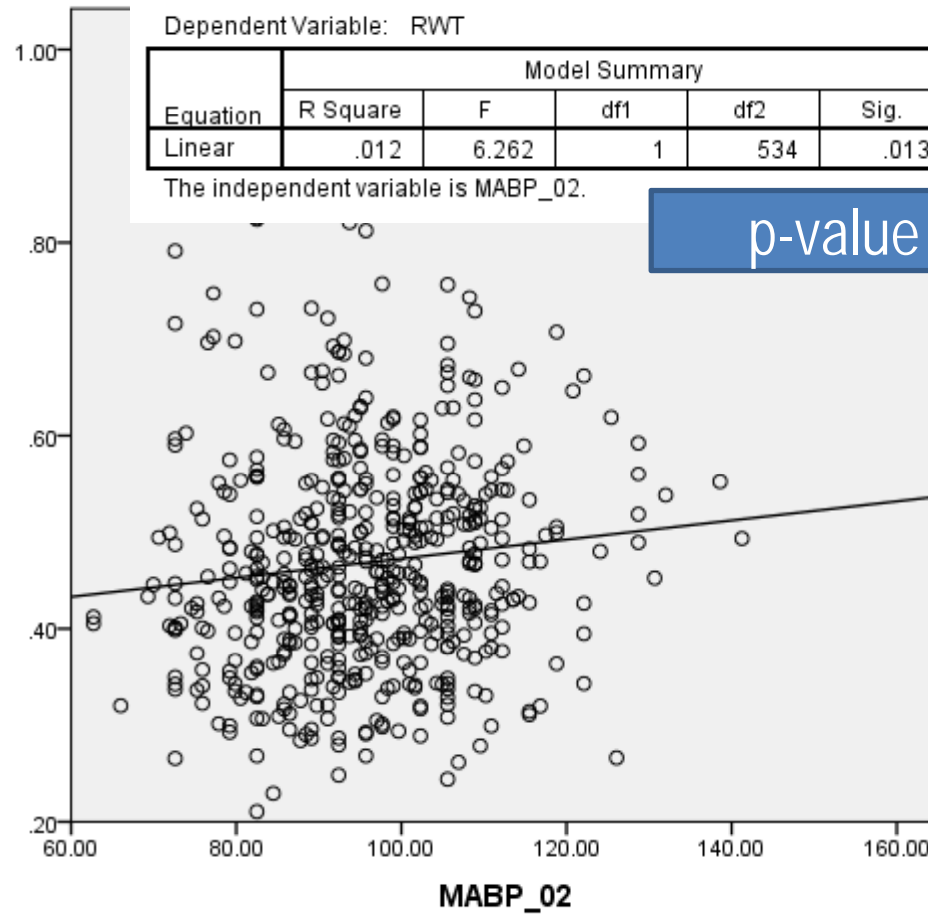
p-value = 0.123
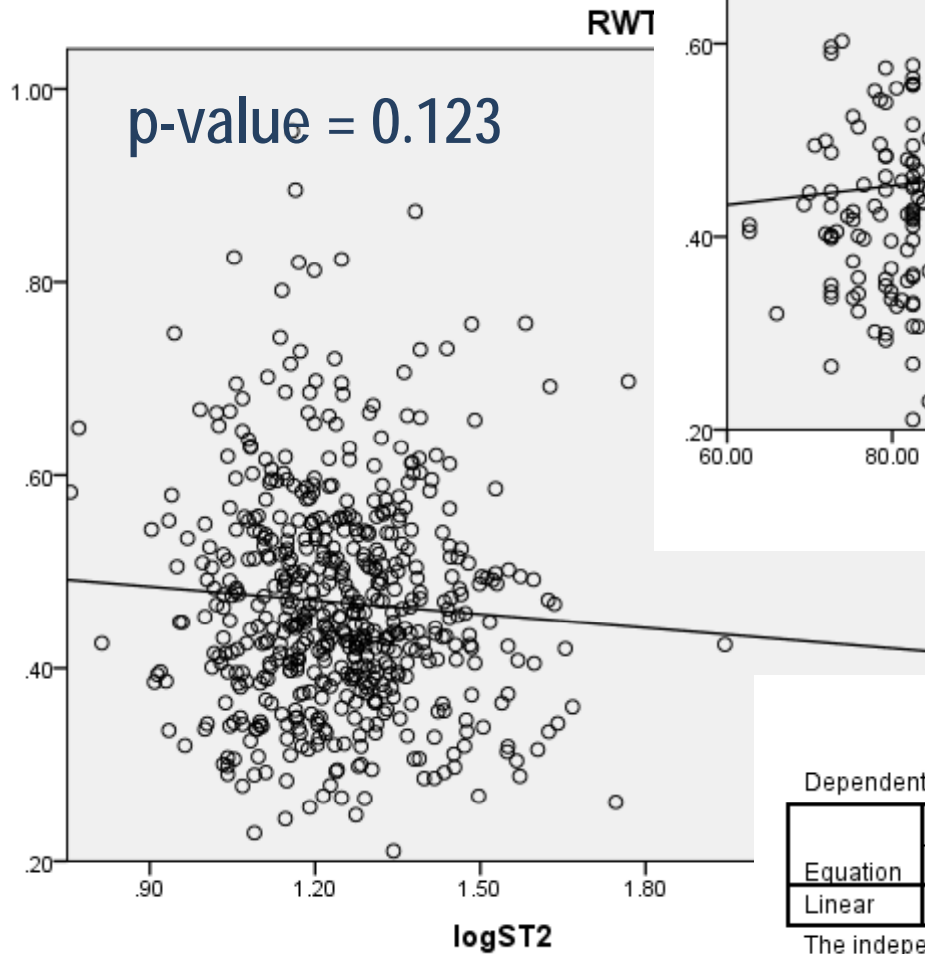
Model Summary and Parameter Estimates

Dependent Variable: RWT

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.004	2.384	1	542	.123	.528	-.048

The independent variable is logST2.
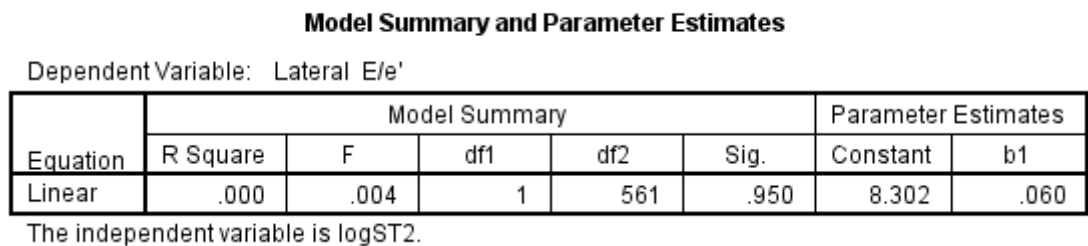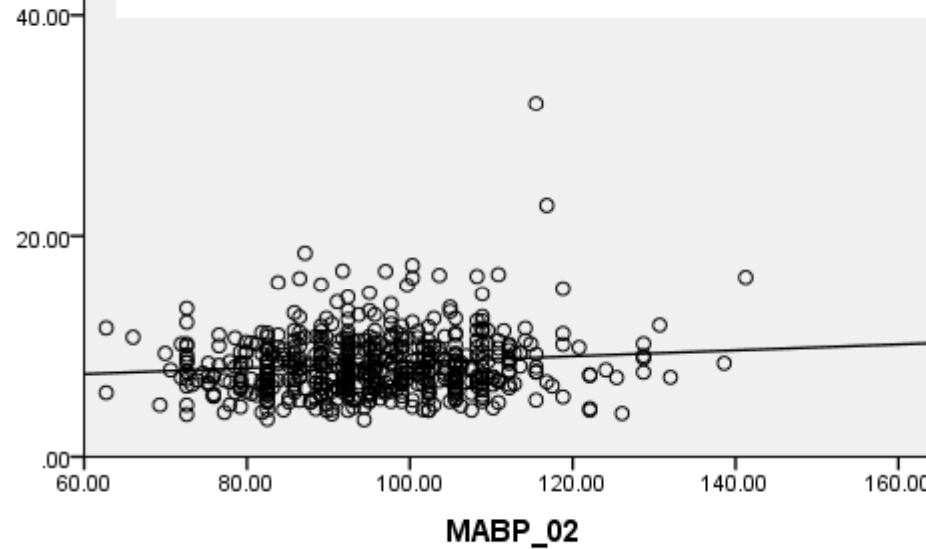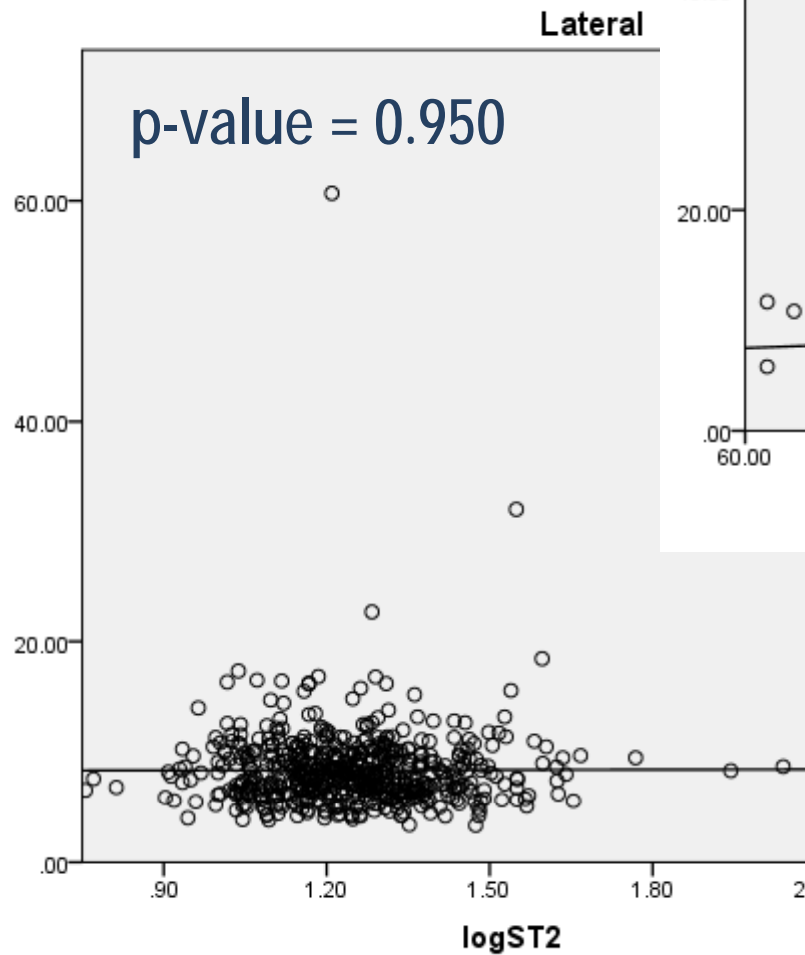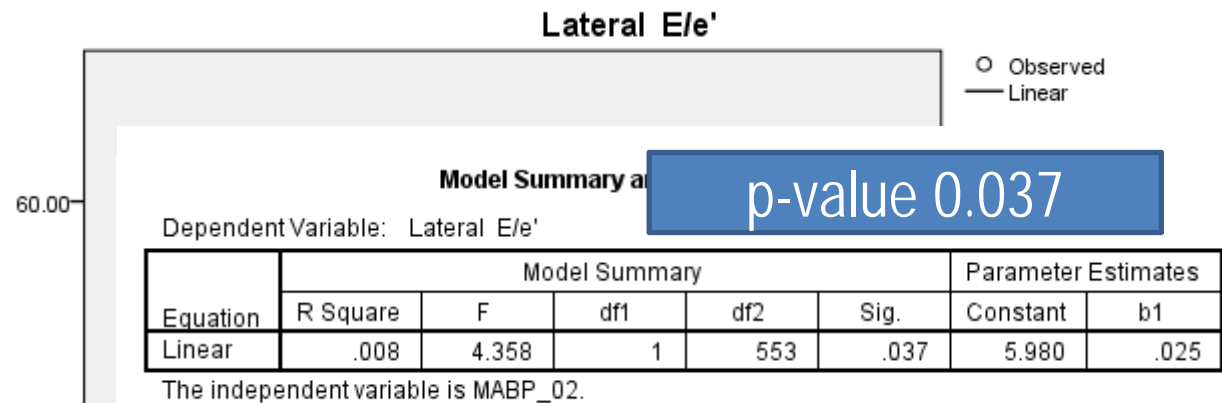
Lateral E/e'

p-value 0.037

p-value = 0.950

Lateral E/e'

Model Summary and Parameter Estimates

Dependent Variable: Lateral E/e'

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.008	4.358	1	553	.037	5.980	.025

The independent variable is MABP_02.

Model Summary and Parameter Estimates

Dependent Variable: Lateral E/e'
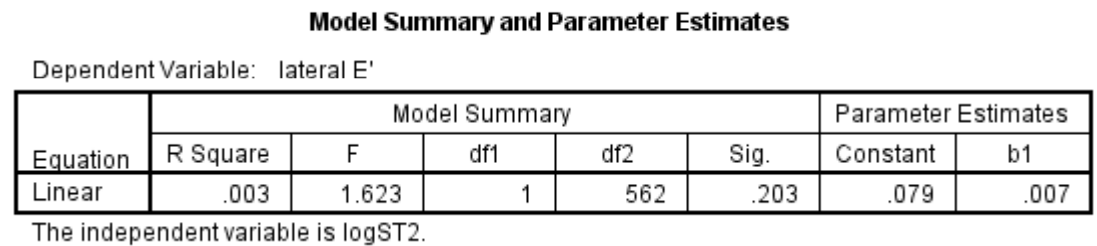
Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.000	.004	1	561	.950	8.302	.060

The independent variable is logST2.

Lateral e′

lateral E'

○ Observed
— Linear

p-value 0.004

Model Summary

Dependent Variable: lateral E'

Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.015	8.562	1	554	.004	.109	.000

The independent variable is MABP_02.

MABP_02

lateral

p-value = 0.203

logST2

Model Summary and Parameter Estimates

Dependent Variable: lateral E'
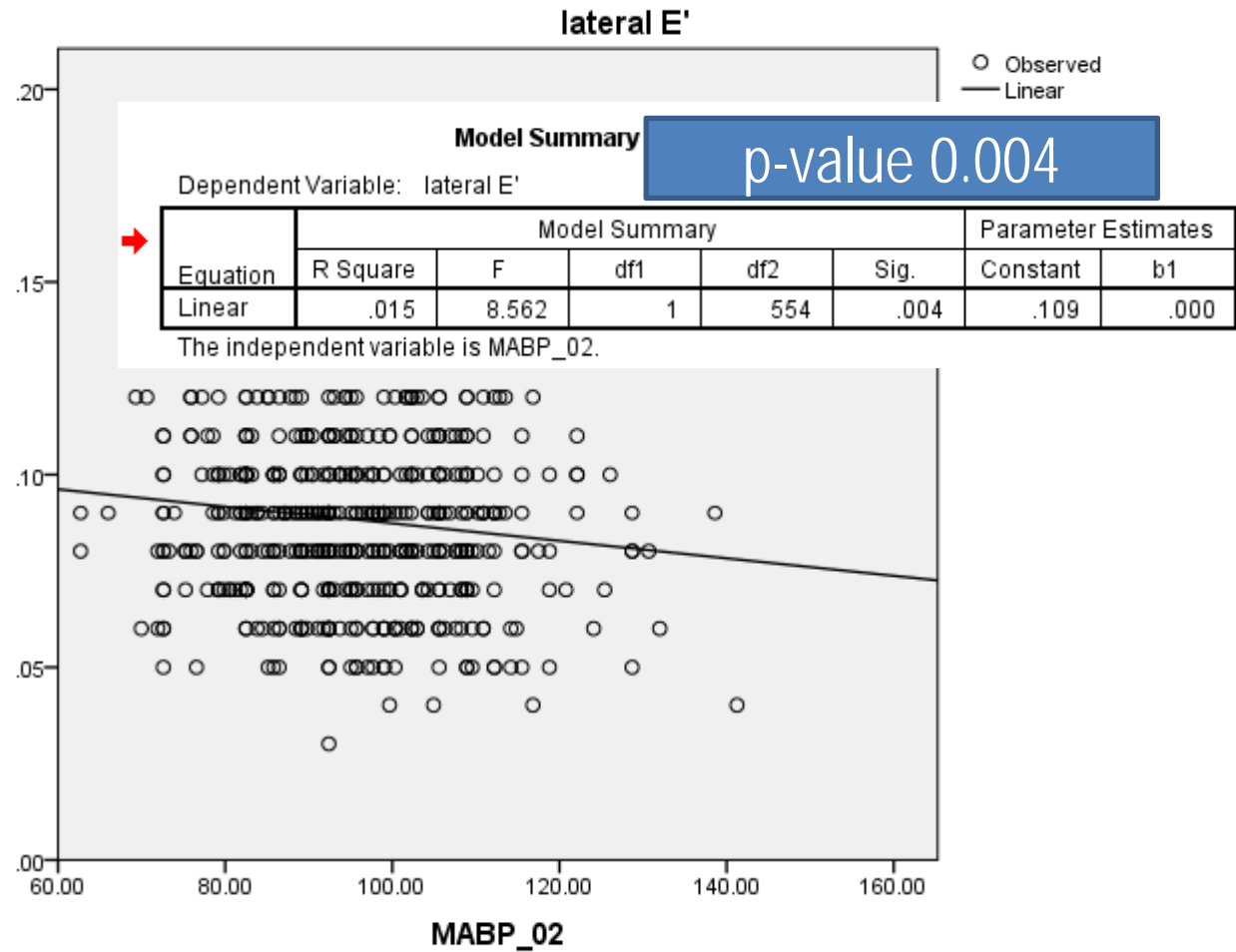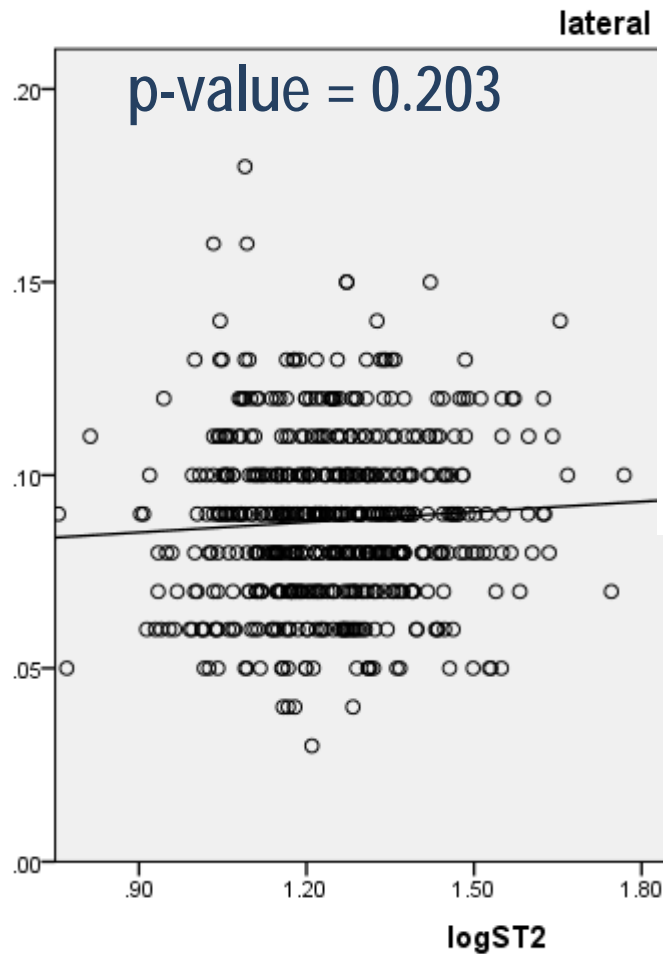
Equation	Model Summary					Parameter Estimates	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	.003	1.623	1	562	.203	.079	.007

The independent variable is logST2.

Conclusion

- Unlike hypertension, sST2 did not demonstrate its predictive value for left ventricular remodeling in 10 years period of follow-up.