

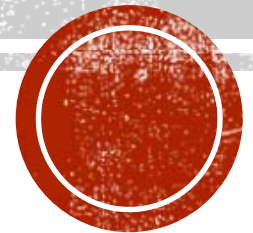
THE STUDY OF SOLUBLE ST2 IN HIGH RISK PATIENTS AND COMPOSITE CARDIOVASCULAR OUTCOMES

Somluck Ninwaranon, MD

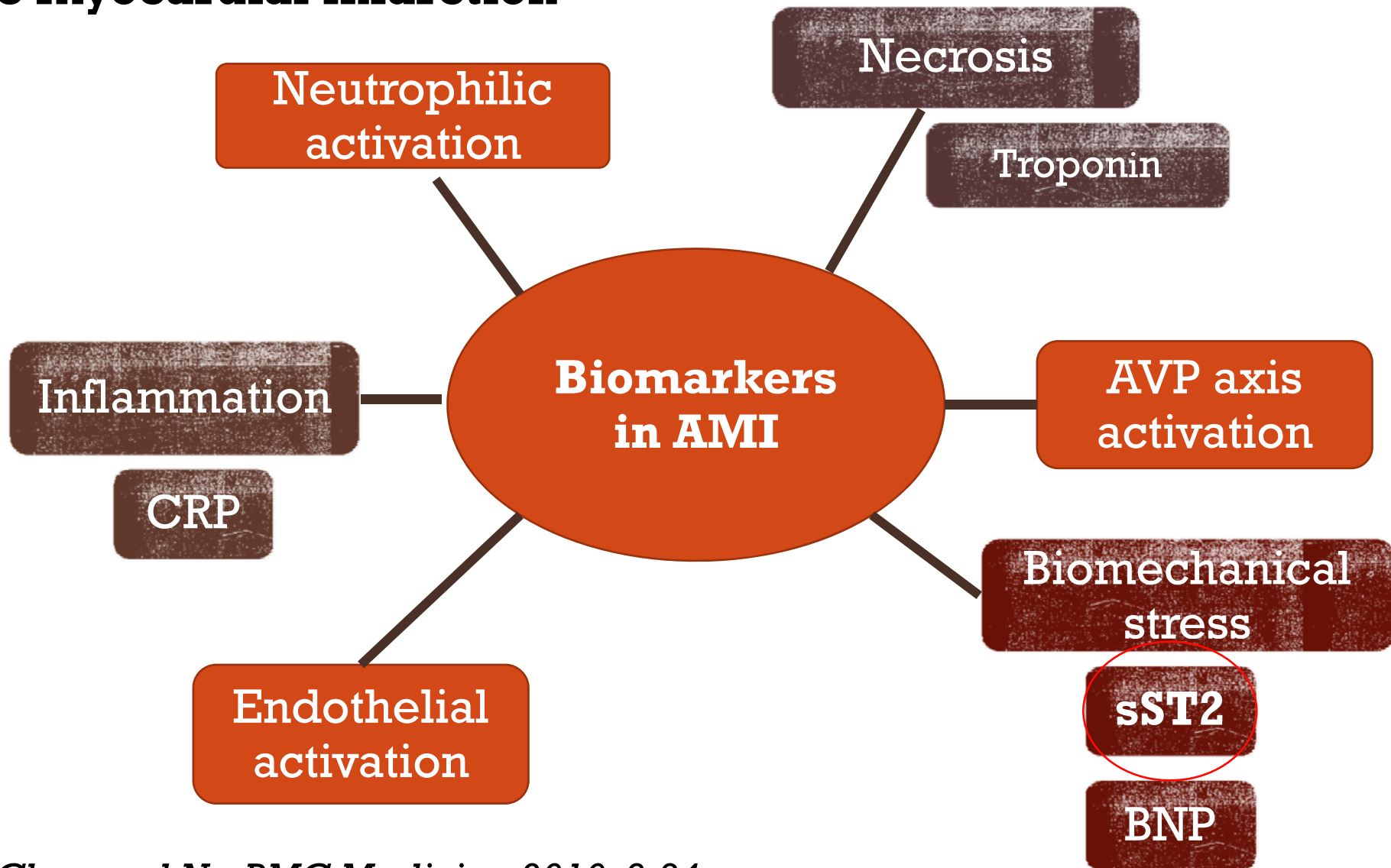
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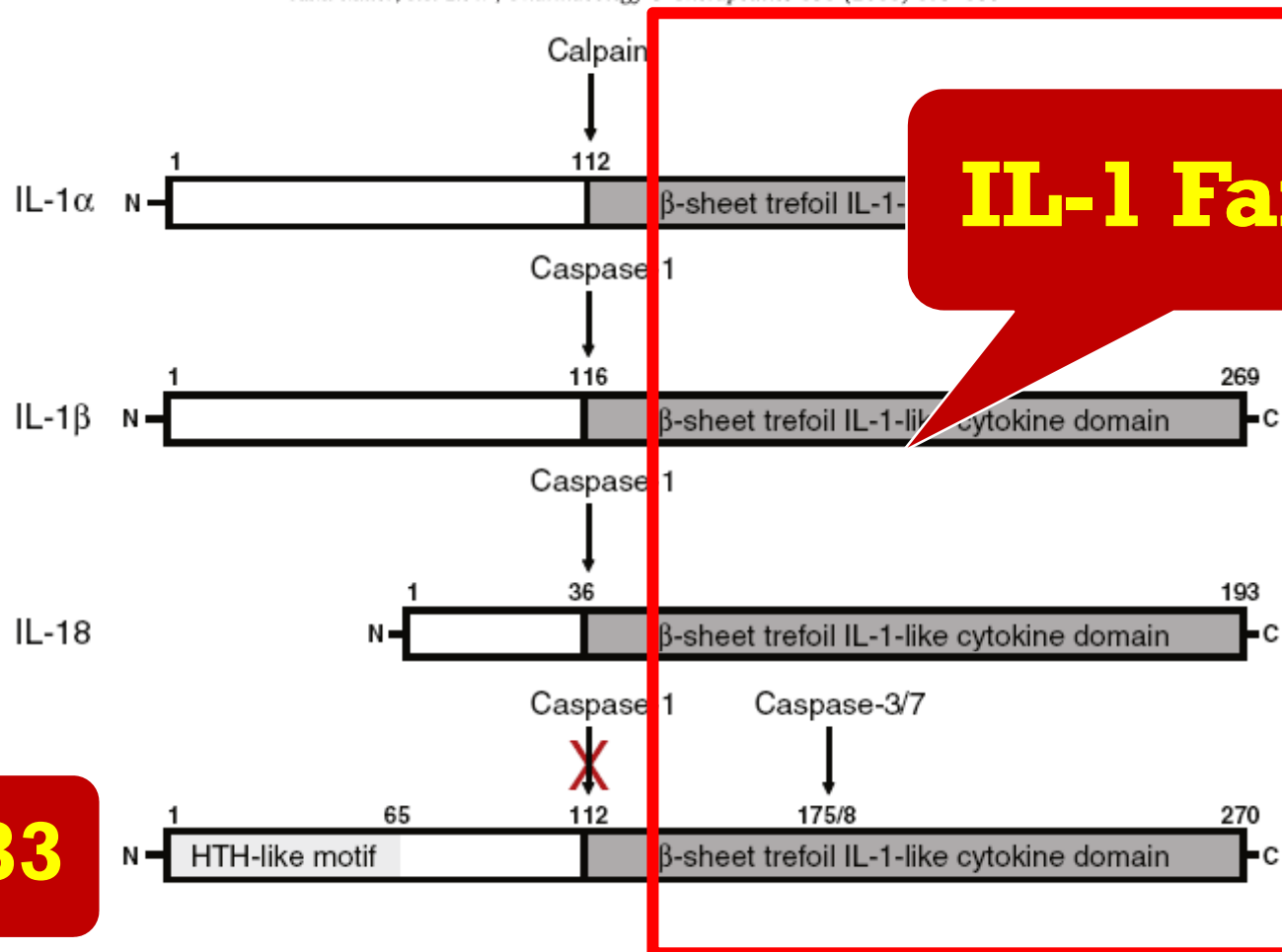


**markers associated with various
hophysiology process associated
h acute myocardial infarction**



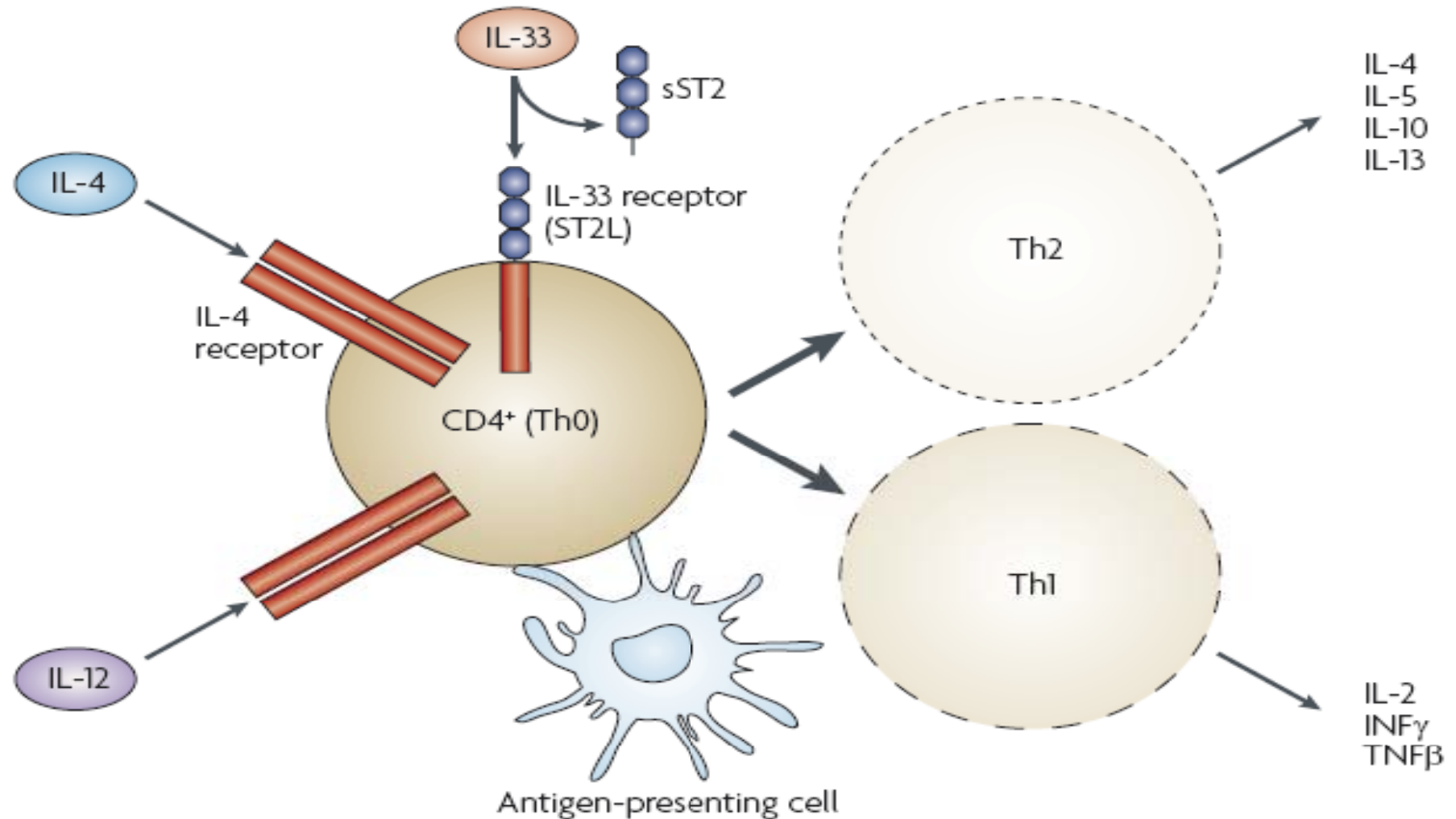
BACKGROUND

A.M. Miller, F.Y. Liew / Pharmacology & Therapeutics 131 (2011) 179–186

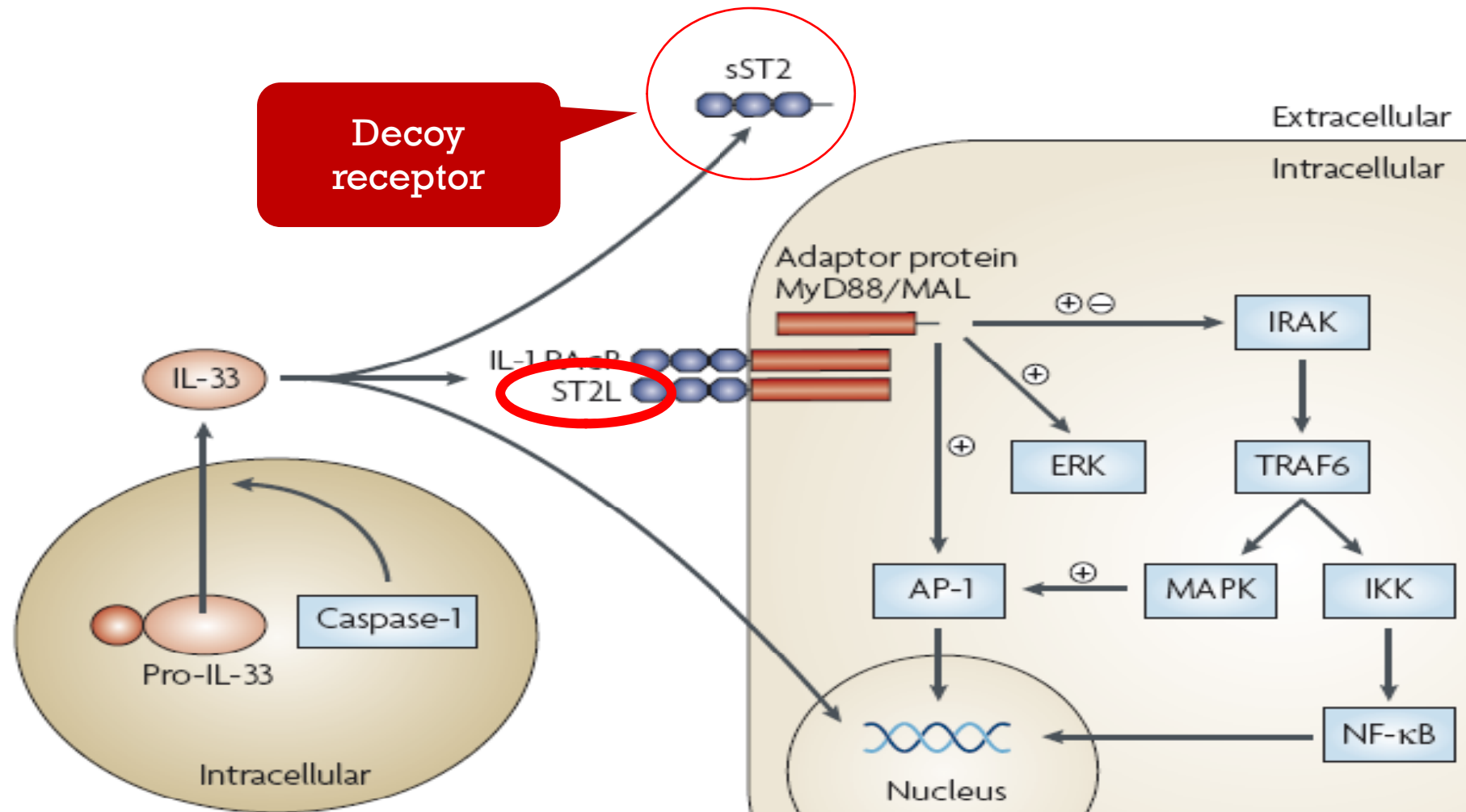


IL-33

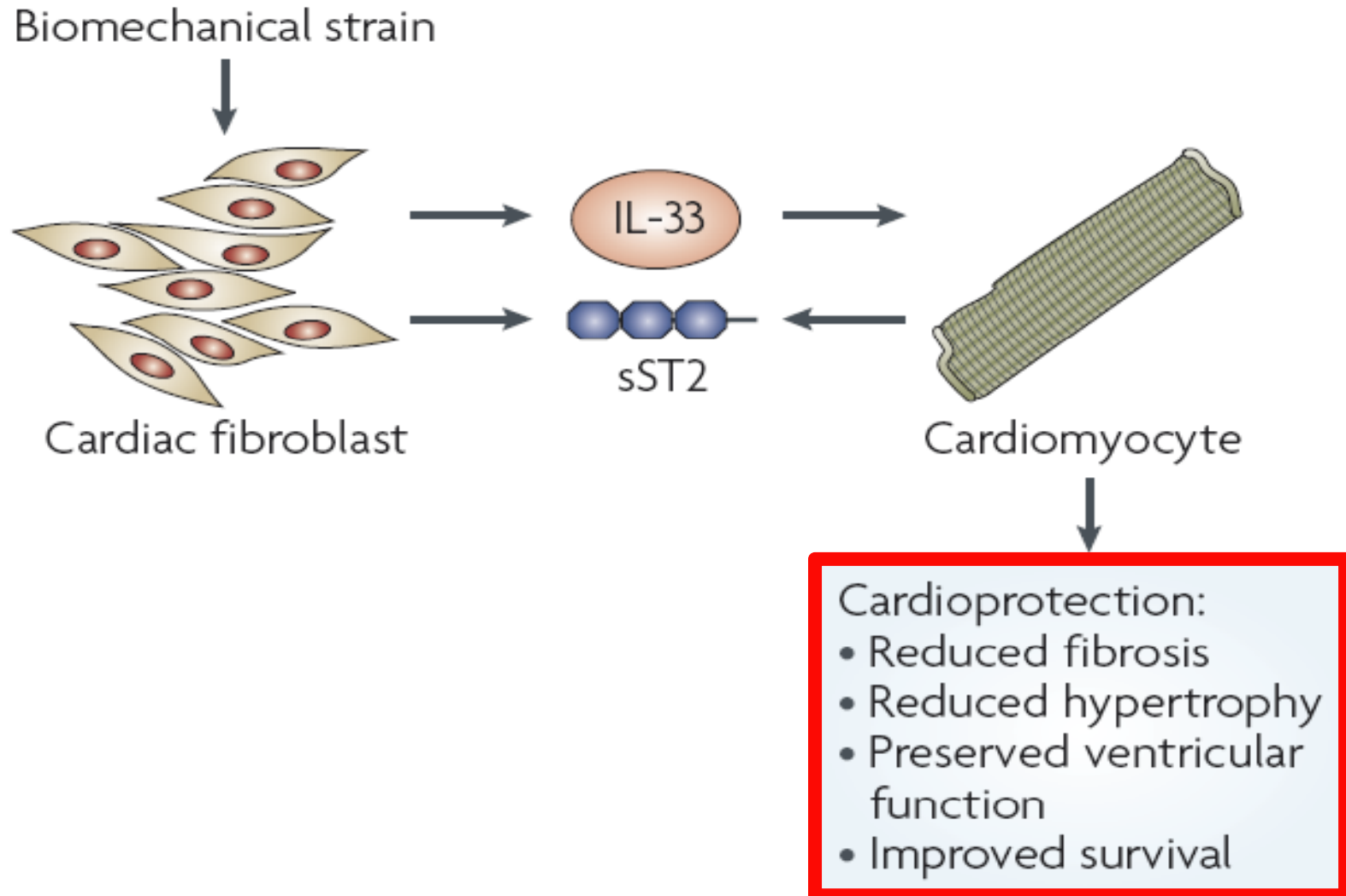
IL-33 in the type 2 immune response



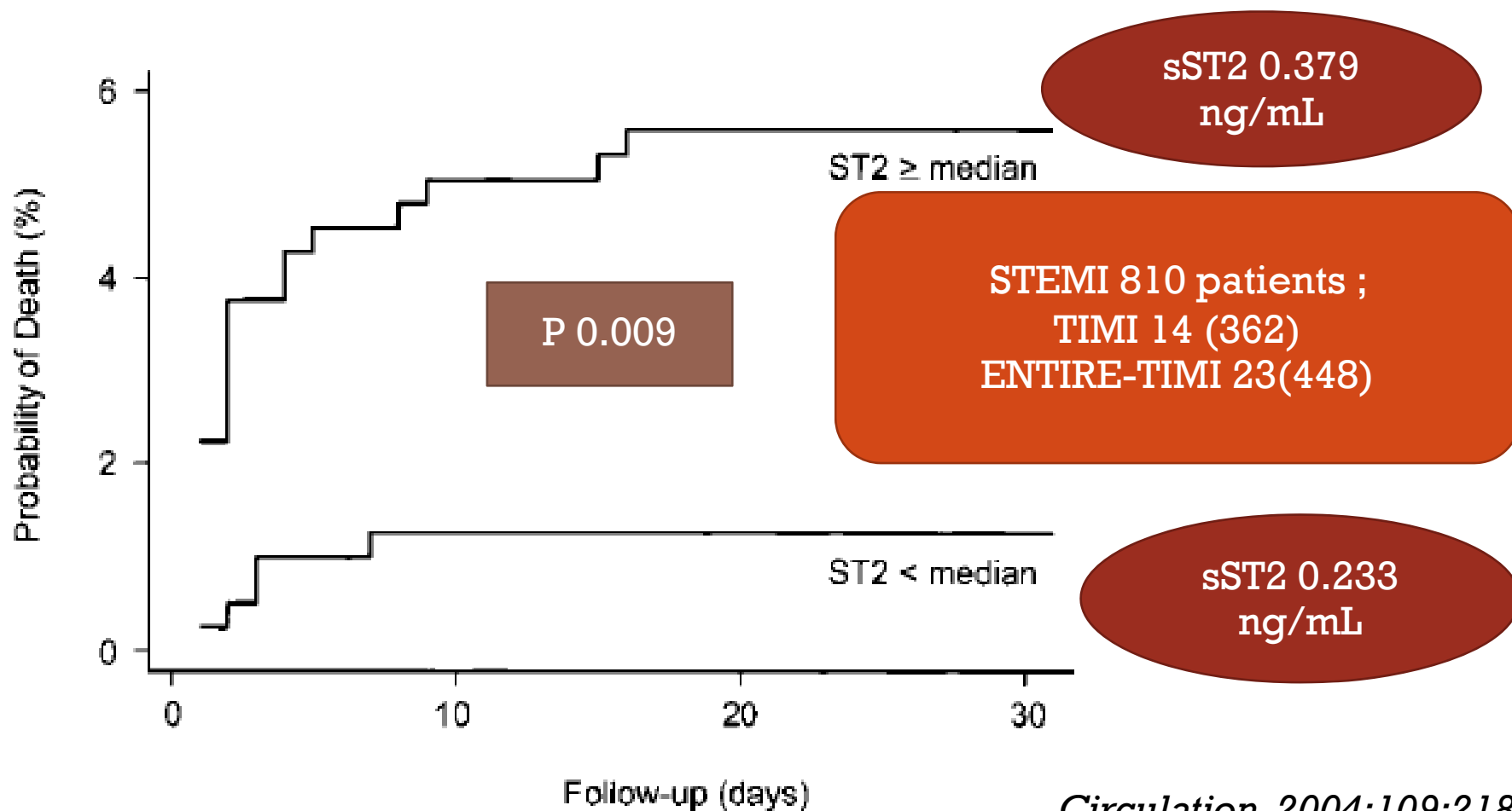
A model for IL-33/sT2 signaling



Cardioprotection of IL-33/sT2



SERUM LEVELS OF THE INTERLEUKIN-1 RECEPTOR FAMILY MEMBER ST2 PREDICT MORTALITY AND CLINICAL OUTCOME IN AMI



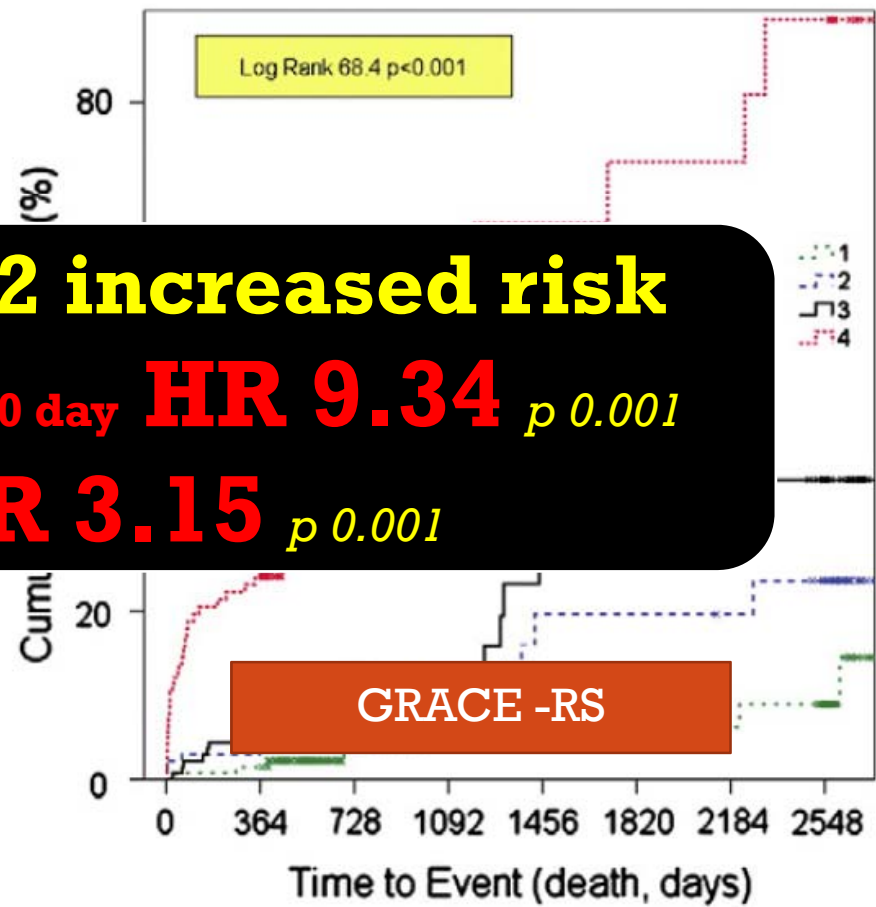
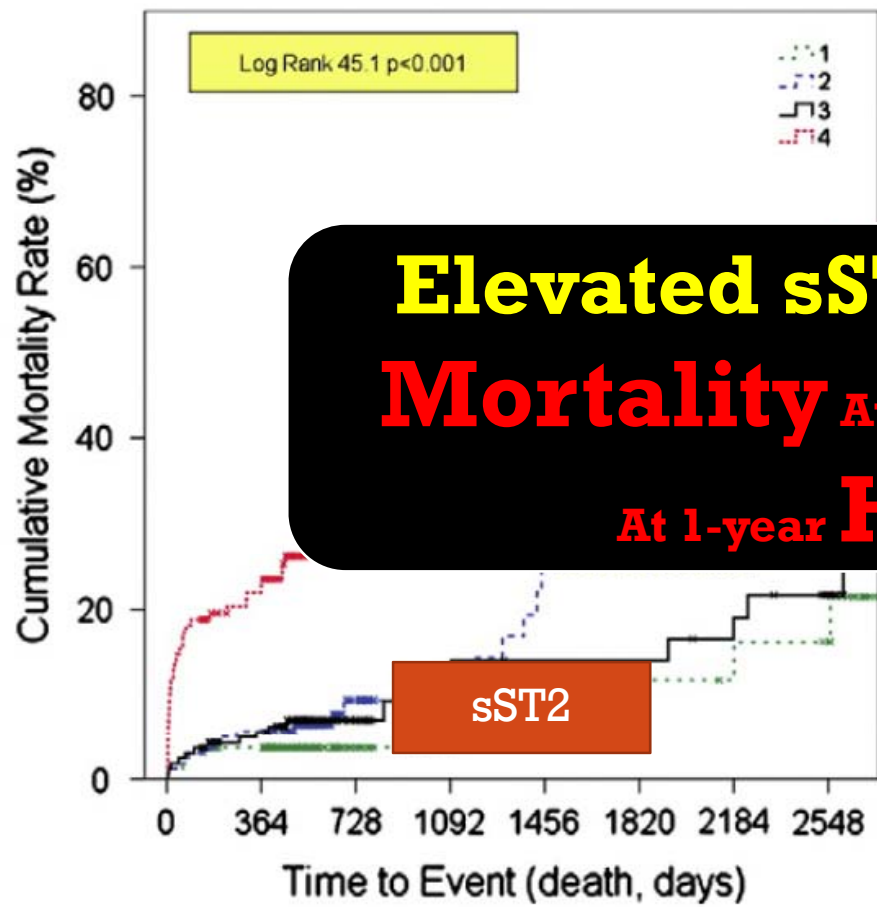
SERUM LEVELS OF THE INTERLEUKIN-1 RECEPTOR FAMILY MEMBER ST2 PREDICT MORTALITY AND CLINICAL OUTCOME IN AMI

TABLE 4. Association Between Baseline ST2 Quartiles and Outcomes

Outcome	Quartile 1, %	Quartile 2, %	Quartile 3, %	Quartile 4, %	P_{trend}	P Q4 vs Q1
In-hospital						
Death	0.98	1.5	3.0	6.4	0.0008	0.003
Recurrent MI	4.4	3.5	0.5	1.5	0.02	0.07
Death/CHF	2.5	4.0	6.4	8.9	0.002	0.004
30-Day						
Death	0.98	1.5	4.0	7.4	0.0001	0.001
MI	5.4	4.5	2.5	2.0	0.04	0.1
CHF	1.5	3.0	5.5	4.0	0.08	0.1
Death/CHF	2.5	4.0	8.9	10.4	0.0002	0.001

MI indicates myocardial infarction; CHF, congestive heart failure.

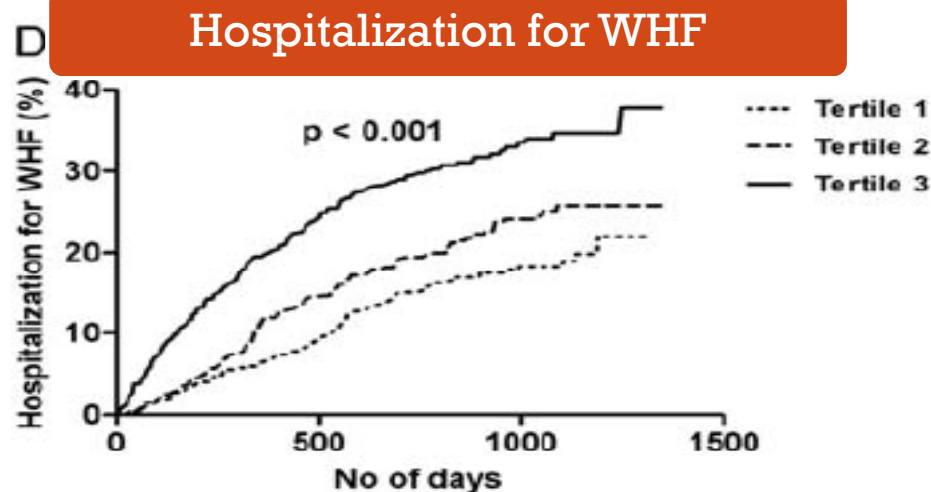
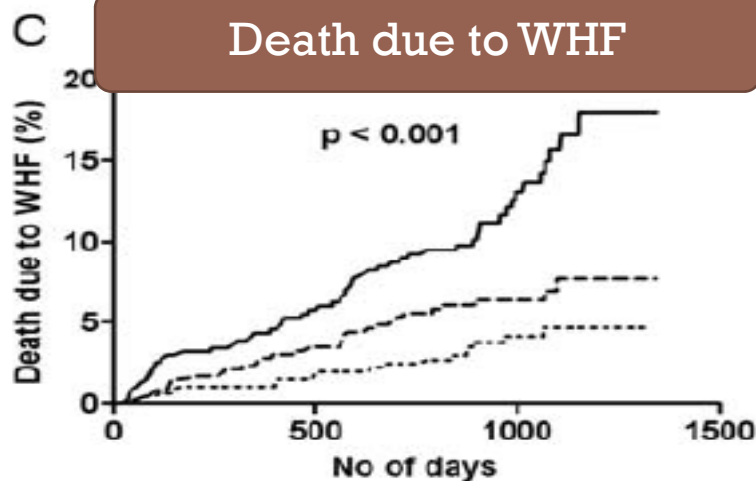
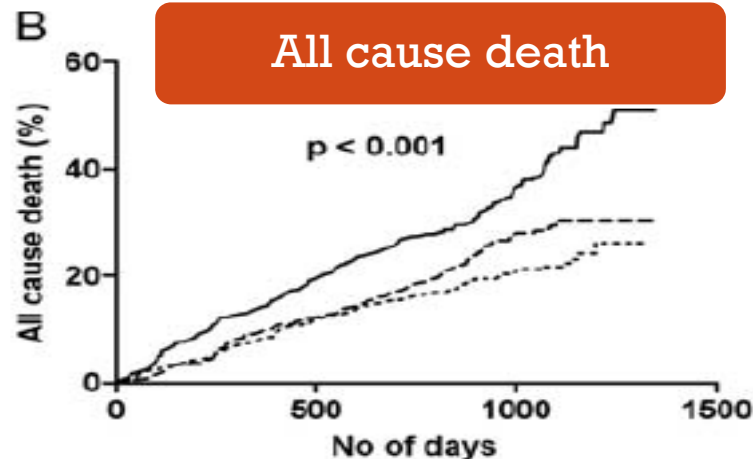
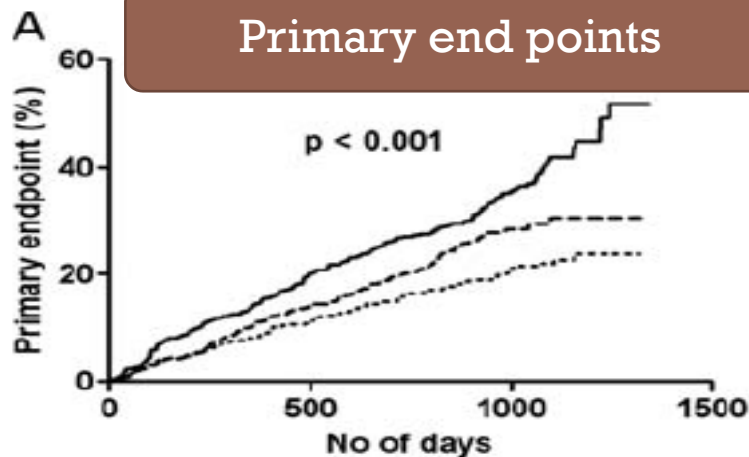
PRE-DISCHARGE RISK STRATIFICATION IN UNSELECTED STEMI: IS THERE A ROLE FOR ST2 OR ITS NATURAL LIGAND IL-33 WHEN COMPARED WITH CONTEMPORARY RISK MARKERS?



Elevated sST2 increased risk
Mortality At 30 day **HR 9.34** $p 0.001$
At 1-year **HR 3.15** $p 0.001$

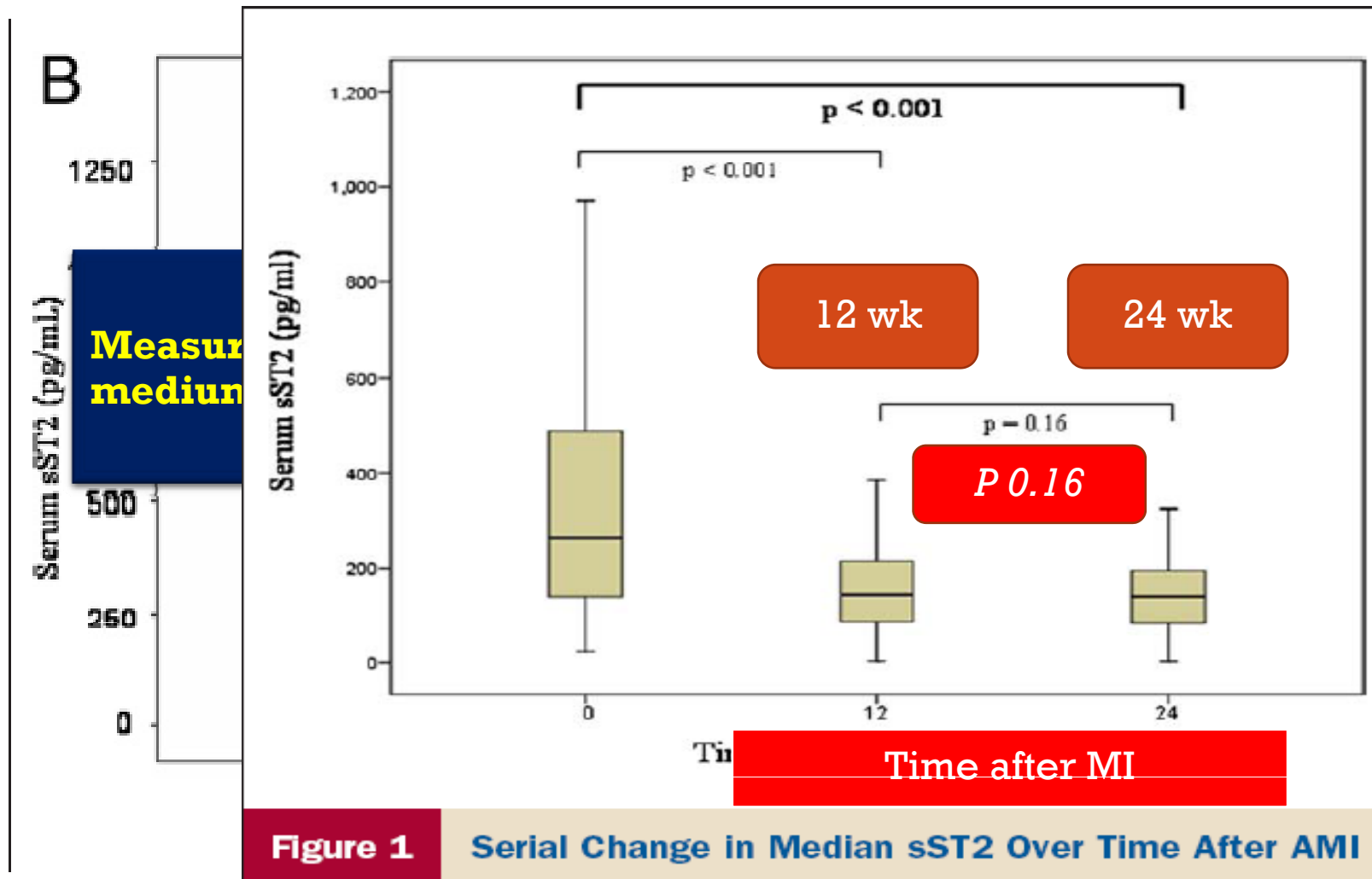
STEMI 677 patients

SOLUBLE ST2 IS ASSOCIATED WITH ADVERSE OUTCOME IN PATIENTS WITH HEART FAILURE OF ISCHAEMIC AETIOLOGY



CORONA study 1,449 pts

Serum soluble ST2 : A Potential Novel Mediator in LV and Infarct Remodeling After AMI



RESEARCH QUESTION



- Is the level of soluble ST2 in stable high risk CV patients association with MACE ?

OBJECTIVES

Finding association between sST2 & cardiovascular outcomes.

Describe sST2 in stable high risk CV patients.

STUDY DESIGN : PROSPECTIVE COHORT

Inclusion

- Age > 45 years
- Coronary artery disease
- Risk ≥ 3 in 7
 - HT
 - Diabetes
 - DLP
 - CKD
 - Smoking
- Male age > 55 years, female age > 65 years
- Family history of premature atherosclerosis

Exclusion

- Refuse to inform & consent
- Studied in others double blind clinical controlled trial .
- Large aortic dissection that be planned to surgery
- Life expectancy < 3 years
- Underlying disease; asthma, rheumatoid arthritis, sepsis

CORE study is cohort study of evaluate cardiovascular events in high cardiovascular risk patients

METHOD

Substudy
CORE

High cardiovascular risk patients
N= 341 patients

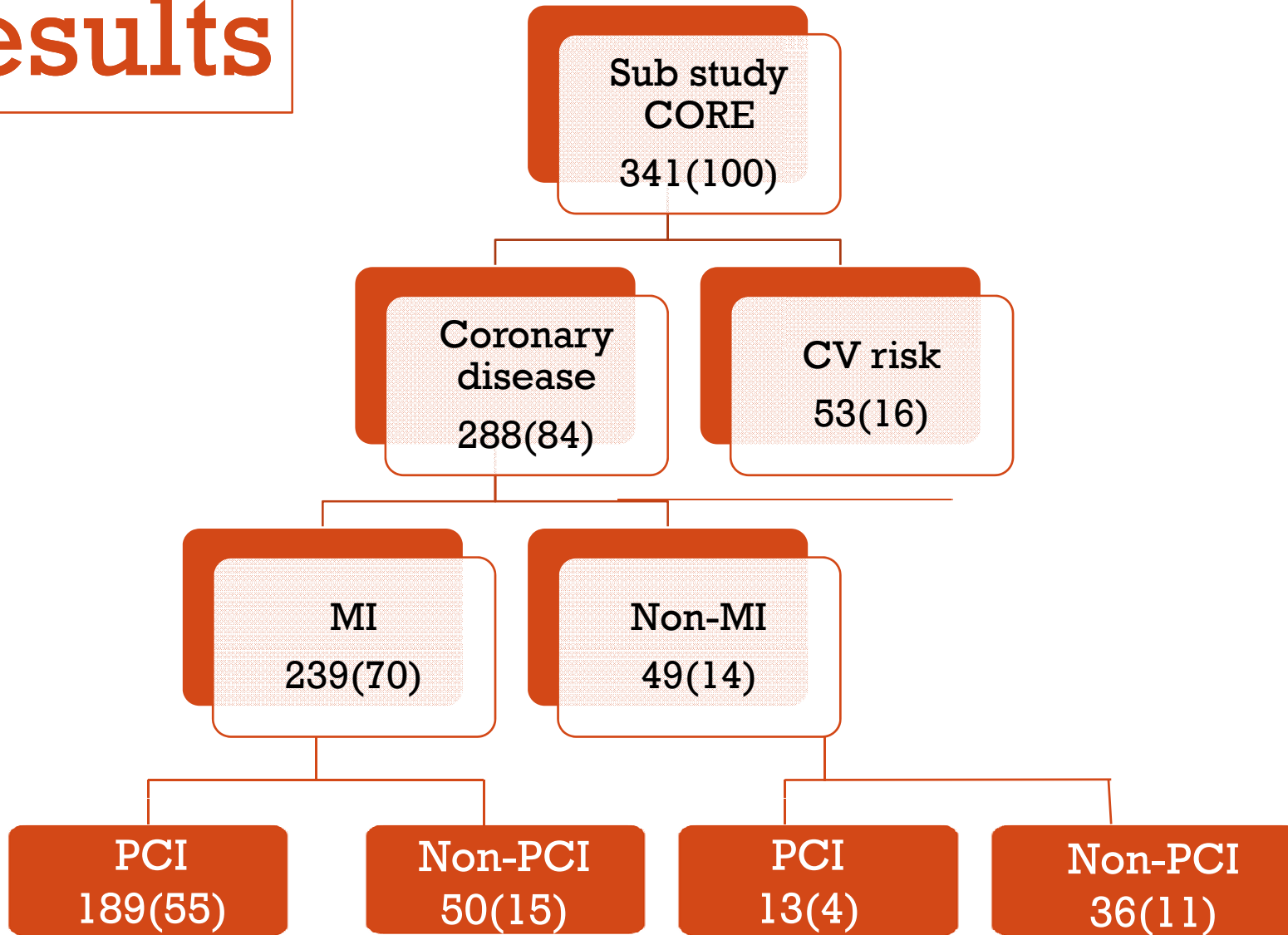


341 patients from 3 sites in
Thai medical school hospitals
(Ramathibodi, Chiangmai and Srinagarind)



- Inform consent after doctor explain the study protocol
- Blood sample for sST2
- Cardiovascular history as in protocol at 0, 6 & 12 months

Results



Baseline characteristic	N=341(%)
Age, year (mean±SD)	65 ± 10
Sex ; Male	206 (59)
Body weight, kg (mean±SD)	63 ± 13
Height, cm (mean±SD)	159 ± 8
Waist circumference, cm(mean±SD)	86 ± 12
Hypertension	241 (71)
Diabetes	145 (43)
Chronic kidney disease	60 (18)
Renal replacement therapy	4 (1)
Kidney transplantation	1 (0.3)
Dyslipidemia	230 (67)
Smoking	25 (7)
Male elder 65 year, female elder 55 year	246 (72)
Family history of premature CAD	24 (7)

Baseline characteristic	N=341 (%)
High risk CV without CAD	53 (16)
Chronic stable angina	44 (13)
Myocardial infarction	239 (70)
Unstable angina	17 (5)
Stroke	19 (5)
Transient ischemic attack	3 (0.9)
Aortic dissection	3 (0.9)
Peripheral arterial disease	5 (1)
Percutaneous coronary artery intervention	202 (59)
Coronary artery bypass	15 (4)

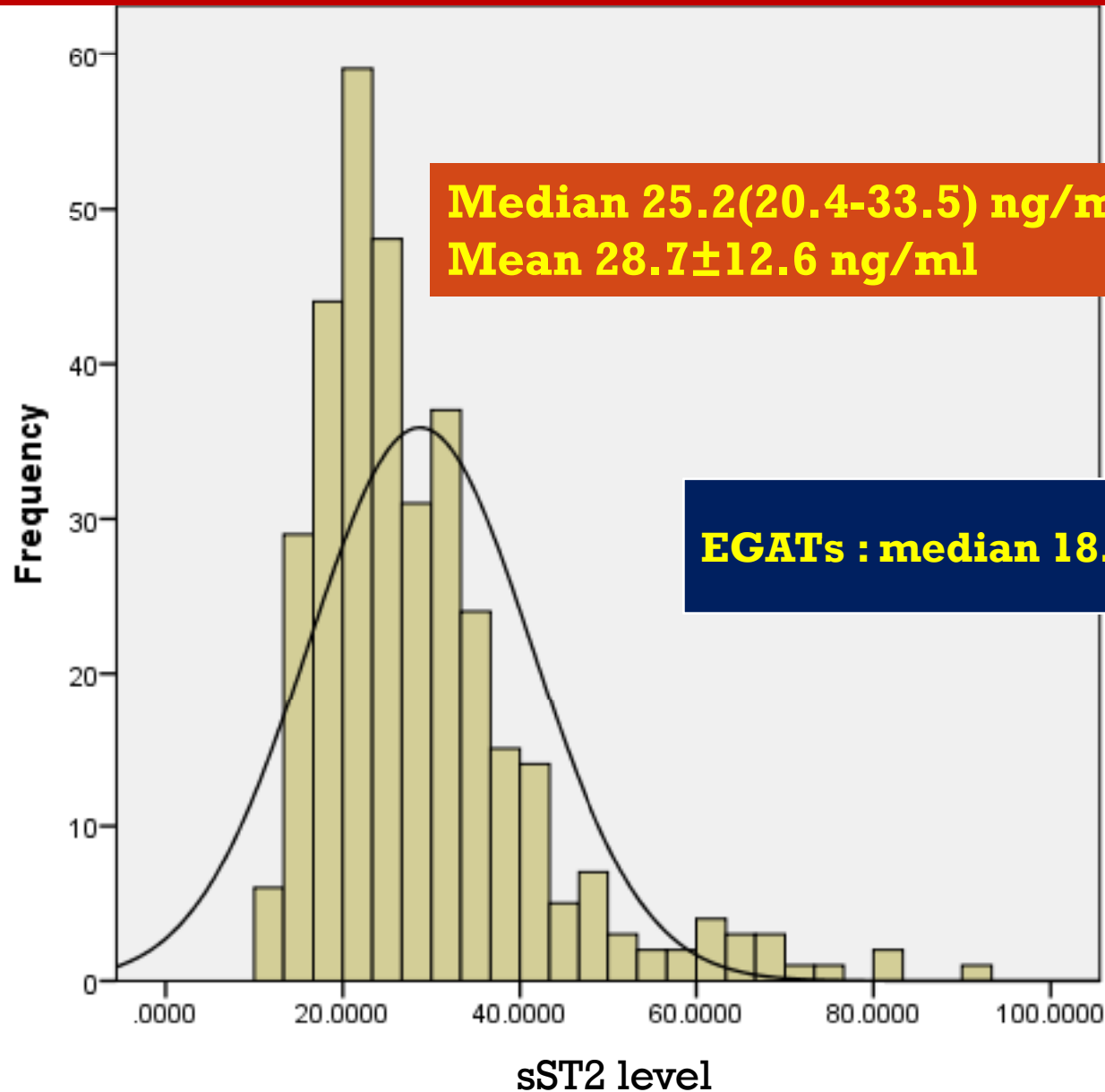
Medication	N=341 (%)
Antiplatelet	325 (95)
ASA	301(88)
Clopidogrel	190(56)
Ticargrelor	1(0.3)
Warfarin	20(6)
Cilostasol	3(1)

Antihypertensive	N=341(%)
Beta-blocker	282(83)
ACEI	135(40)
ARB	105(31)
Ca-blocker	120(35)
Nitrate	144(42)
diuretic	85(25)

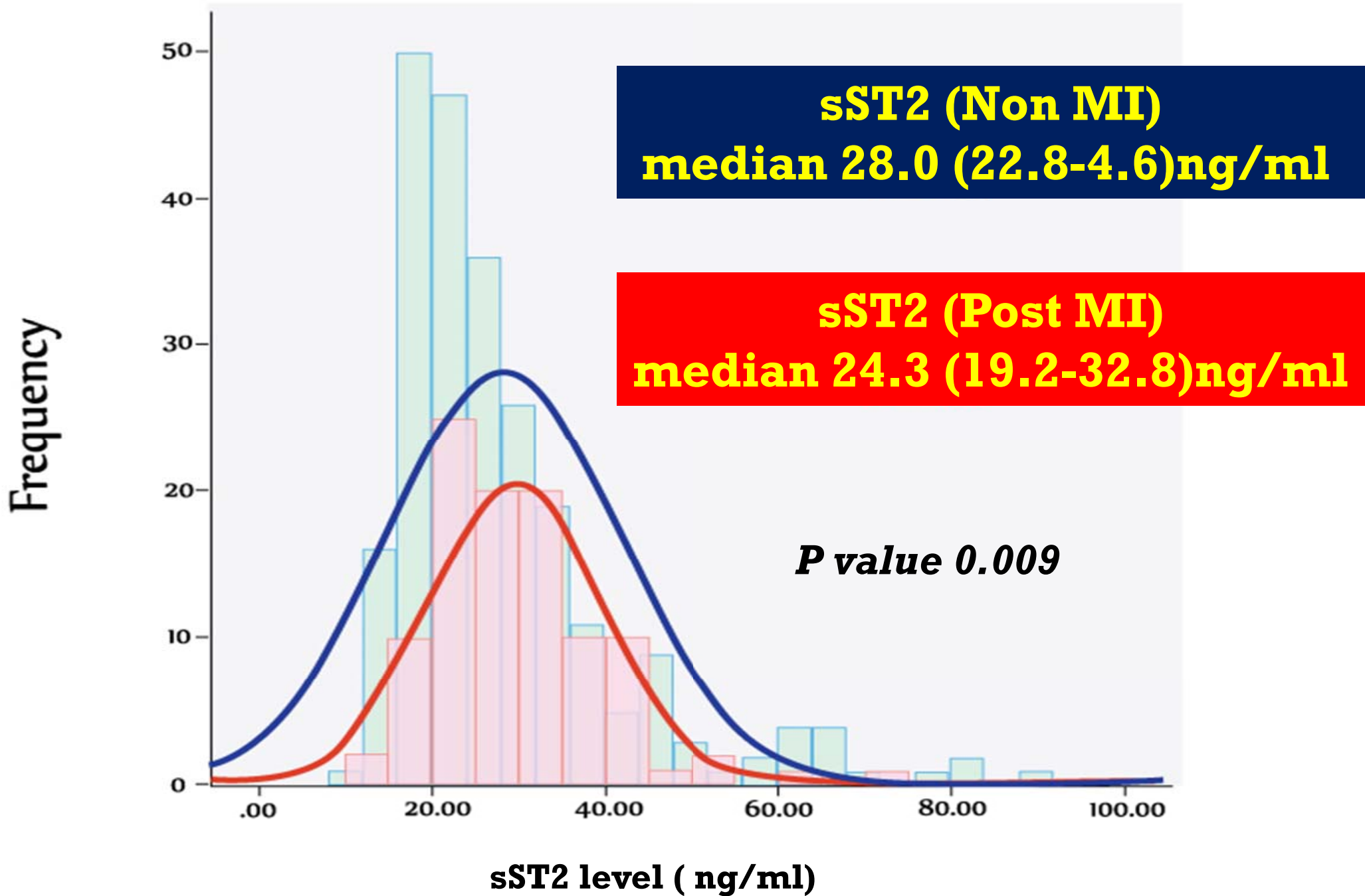
Medication	N=341(%)
Anti-lipid agent	328(96)
Statin	328(96)
Fibrate	13(4)
Niacin	4(1)
Ezetimibe	20(6)

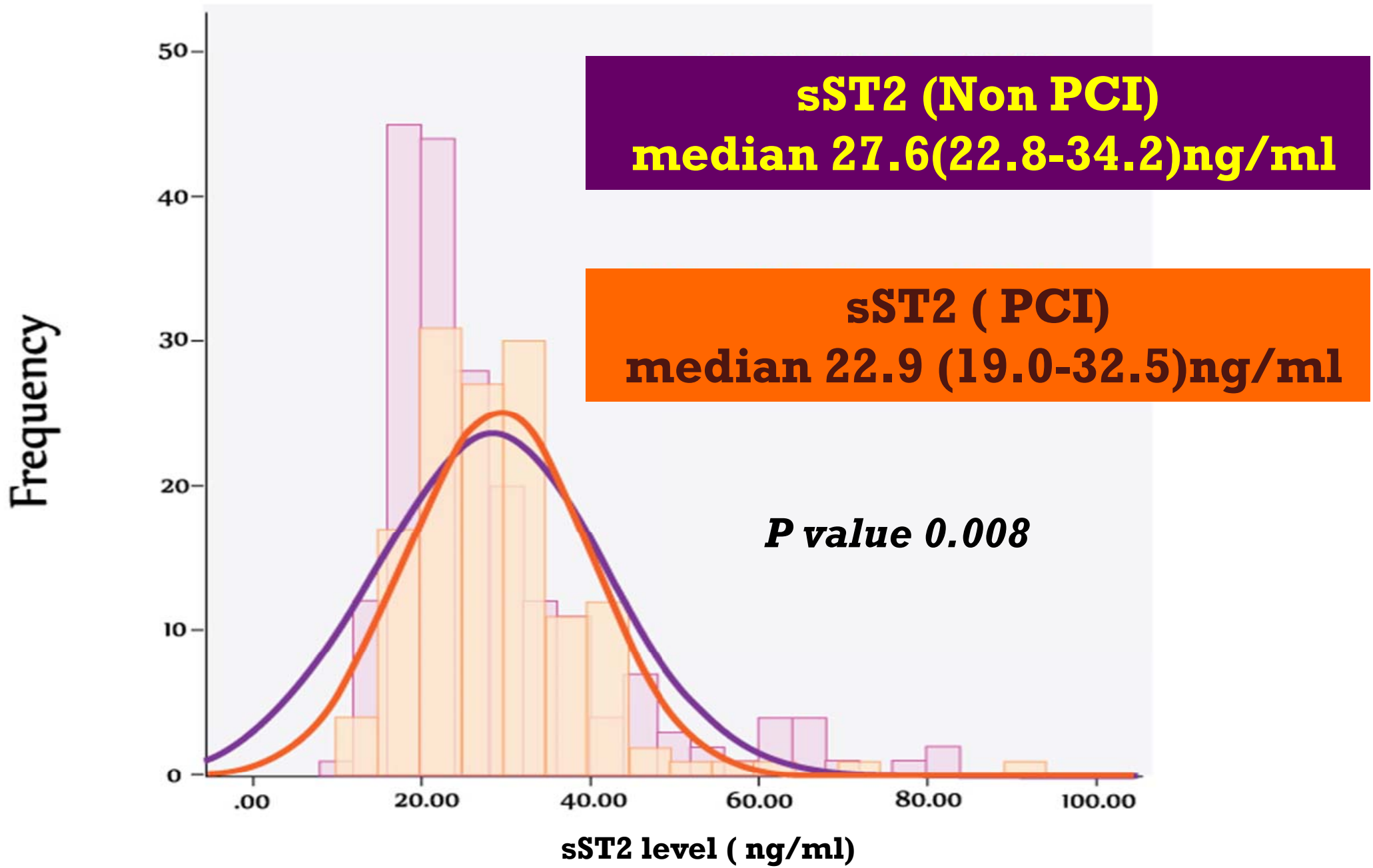
Medication	N=341(%)
Diabetic agent	123(36)
Insulin	21(6)
Sulfonylurea	70(21)
Biguanide	92(27)
Thiazolidinedione	7(2)
DPP4I	14(4)

sST2 level in stable high risk CV patients

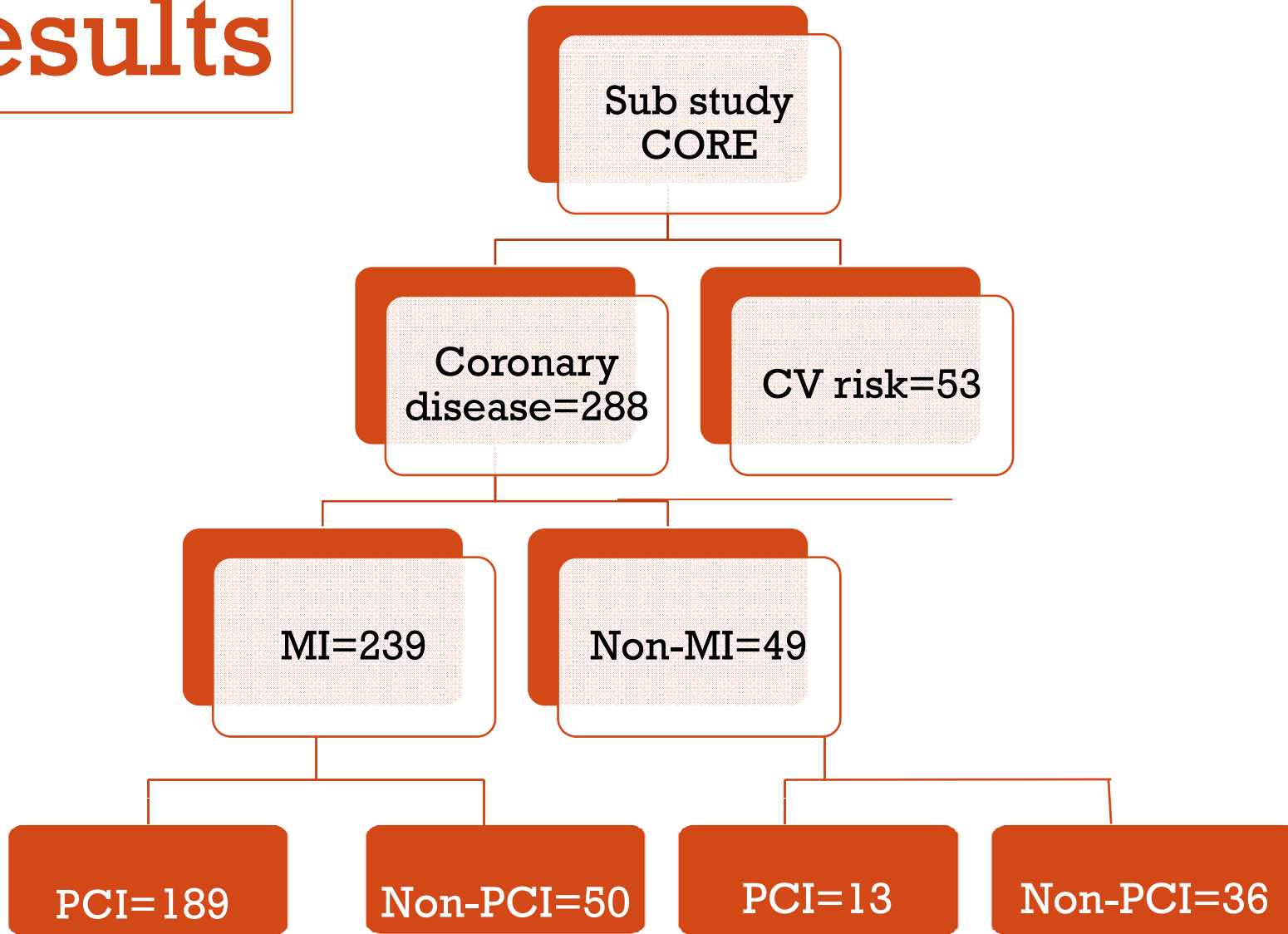


¹A study of sST2 and hsCRP in a population-based cohort : Thai EGAT study, Poh Chanyavanich, MD





Results



	DM (N=147)	Non-DM (N=204)	P-value
sST2 median (interquatile)	26.6(14.6)	24.3(13.7)	0.012
	HT (N=245)	Non-HT (N=106)	P-value
sST2 median (interquatile)	26.7(12.9)	21.9(11.4)	0.000
	CKD (N=62)	Non-CKD (N=289)	P-value
sST2 median (interquatile)	30.2(14.5)	24.7(13.0)	0.001

	DLP (N=236)	Non-DLP (N=115)	P-value
sST2 median (interquatile)	27.1(13.0)	22.5(12.9)	0.000
	Smoking (N=27)	Non-smoking (N=324)	P-value
sST2 median (interquatile)	23.5(9.8)	25.2(13.0)	0.060
	Elderly (N=254)	Non-elderly (N=97)	P-value
sST2 median (interquatile)	25.9(13.3)	23.0(12.3)	0.049

	Male (N=206)	female (N=145)	P-value
sST2 median (interquatile)	25.7(12.5)	24.2(15)	0.045

sST2 level in Post MI & composite outcomes

sST2 level	Composite outcome Negative N(%)	Composite outcome Positive N(%)	Total
Low sST2 < 35 ng/ml	249(92.2)	21(7.8)	270(79.2)
High sST2 ≥ 35 ng/ml	62(87.3)	9(12.7)	71(20.8)
Total N(%)	311(91.2)	30(8.8)	341(100)

P-value 0.195 , Pearson's R

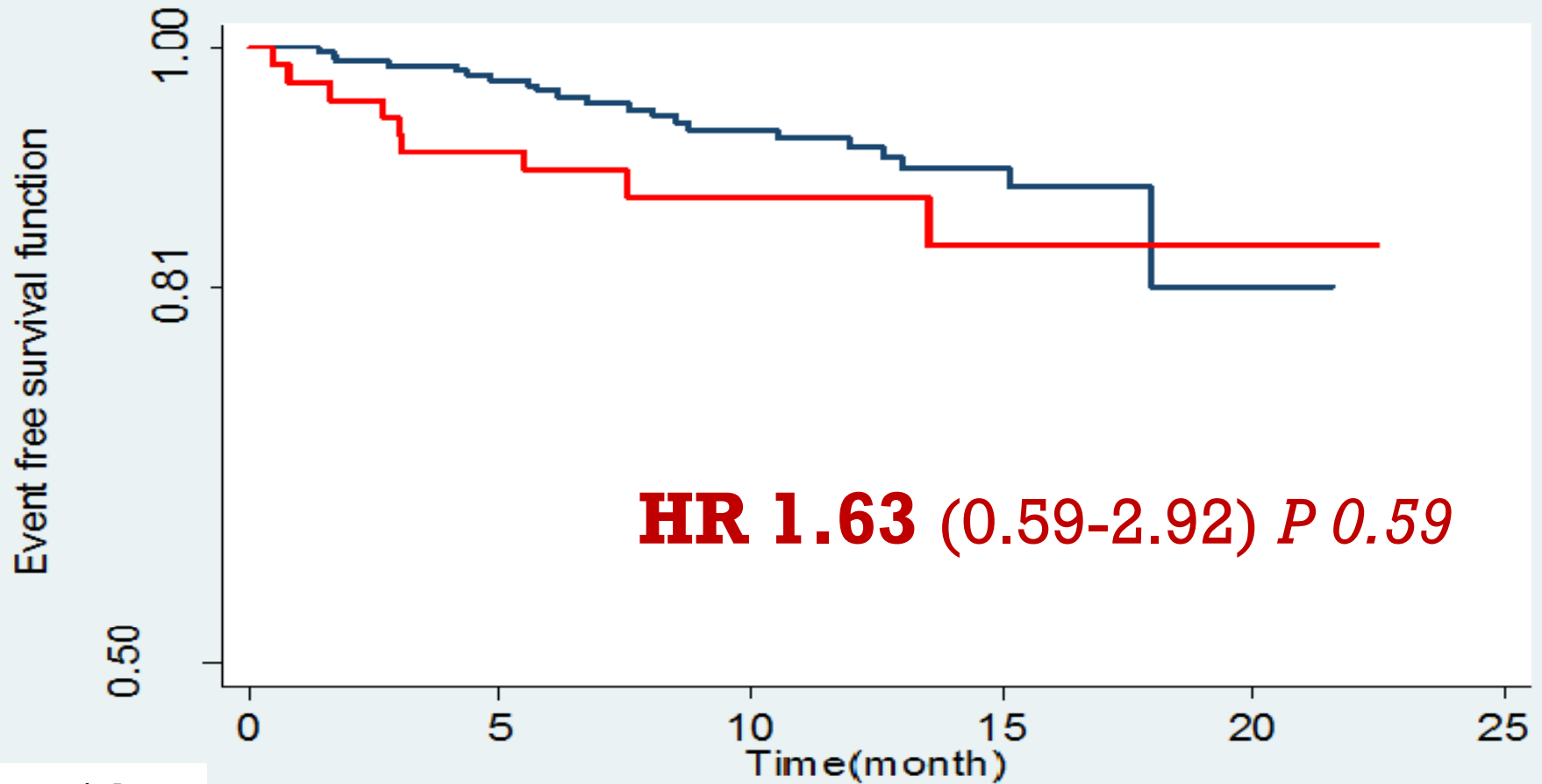
Cut point of sST2 ; 3rd Quartile

Odd ratio
1.73

Table Model fitting by Cox's regression (stepwise selection method)

Independent Variables	<u>Univariate</u>			Multivariate		
	HR	95% CI	P-value	HR	95% CI	P-value
1. Demographic data						
Age≥65 years	1.01	0.49-2.06	0.986			
Male gender	1.60	0.73-3.49	0.240			
Smoking	1.55	0.47-5.13	0.474			
PHx	1.51	0.35-6.45	0.577			
BMI(kg/m ²)	1.18	0.57-2.46	0.647			
2. Underlying disease						
DM	3.13	1.48- 6.61	0.003	2.45	1.12-5.35	0.025
HT	2.14	0.86- 5.29	0.100			
CKD	3.05	1.37- 6.79	0.006	2.40	1.05-5.46	0.037
ARRT	4.40	0.59- 32.65	0.147			
DLP	0.91	0.43- 1.92	0.802			
CSA	2.37	0.96-5.87	0.061	1.85	0.73-4.67	0.194
MI	0.60	0.27-1.36	0.223			
JA	0.75	0.10- 5.49	0.773			
PCI	0.72	0.34-1.52	0.389			
3. Physical examination						
SBP≥140 or DBP ≥ 90 (mmHg)	1.49	0.52-4.28	0.457			
HR≥100/min	3.99	1.20-13.26	0.024	3.30	0.98-11.16	0.055
FEV1 < 55 %	1.85	0.78-4.41	0.165			
4. cardiac biomarker						
NT2 > 35 <u>pg/ml</u>	1.63	0.74- 3.57	0.225	1.31	0.59-2.92	0.59

Univariation of sST2 level and composite events



Number at risk

sST2 < 35 ng/ml

270

250

151

57

8

0

sST2 >= 35 ng/ml

71

62

40

17

6

0

— sST2 < 35ng/ml

— sST2 >= 35ng/ml

CONCLUSION

- In stable high risk patients have higher sST2 level more than normal population(EGAT cohort)



- Median sST2 25.2 ng/ml and 18.39 ng/ml respectively.
- sST2 in **male sex, T2DM, HTN,CKD and DLP** were associated with higher sST2 level.

CONCLUSION

- sST2 in **post myocardial infarction patients who underwent PCI** have **lower** sST2 than non-PCI group.
- ***High sST2 level ≥ 35 ng/ml*** trend to predict higher composite cardiovascular outcomes in stable high risk patients.

CLINICAL APPLICATION

sST2 may be the surrogate outcome for MACE if the physician use it for follow up after optimal medical treatments or new intervention in stable high risk patients.