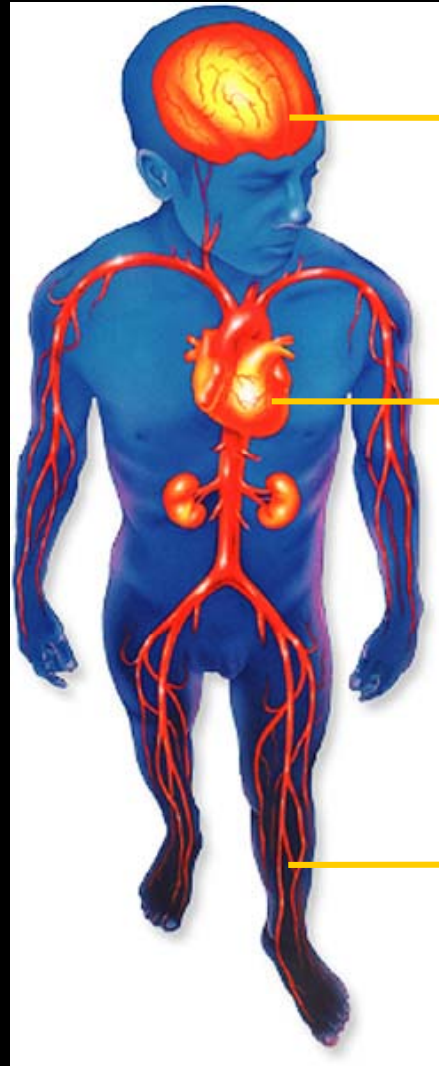# A cohort of patients with high risk for cardiovascular events (CORE-Thailand) :

Preliminary analysis of baseline characteristics

Major Manifestations of Atherothrombosis

Cerebrovascular disease (Cerebrovasc Dis)

Coronary artery disease (CAD)

Peripheral arterial disease (PAD)

1. Viles-Gonzalez JF. *Eur Heart J* 2004; 25: 1197–1207.

Patients with Previous Atherothrombotic Events are at Increased Risk of Further Events

Increased risk versus general population

	MI	Stroke
Ischemic stroke	2–3 X (includes angina and sudden death*)[1]	9 X[2]
MI	5–7 X (includes death)[3]	3–4 X (includes TIA)[1]
PAD	4 X (includes only fatal MI and other CHD death†)[4]	2–3 X (includes TIA)[2]

*Sudden death defined as death documented within one hour and attributed to coronary heart disease (CHD)
†Includes only fatal MI and other CHD death; does not include non-fatal MI

1. Kannel WB. *J Cardiovasc Risk* 1994; 1: 333–339.
2. Wilterdink JI et al. *Arch Neurol* 1992; 49: 857–863.
3. Adult Treatment Panel II. *Circulation* 1994; 89: 1333–1363.
4. Criqui MH et al. *N Engl J Med* 1992; 326: 381–386.

Limitations of the current information in Thailand

- Focused on studying specific risk factors, or 'single' manifestations of the disease (e.g. heart disease)
- Short term follow up
- No study focusing on clinical practice

CORE-Thailand: Objectives

Primary objective:

To determine the incidence of cardiovascular events in high atherosclerotic risk patients

CORE-Thailand: Objectives

Secondary objectives

- To study the atherosclerotic risk factors in Thai population
- To study "real world" practice in treatment of atherosclerotic patients among various level of hospitals
- To study the success rate of risk factor control

Study design

- Prospective cohort study

- Population: Thai patients with high atherosclerotic risk who are currently treated in out patient clinic

- Participating hospitals: university hospitals, tertiary care hospitals, secondary care hospitals

Population

- Patients with age ≥ 45 year old

  - with multiple atherosclerotic risk
  - with established atherosclerotic disease

Population

Established cardiovascular disease

1. Documented cerebrovascular disease Ischemic stroke or TIA

1. Documented coronary disease Angina, MI, angioplasty/ stent/bypass

2. Documented historical or current intermittent claudication associated with ABI <0.9

Multiple (≥ 3)risk factors

1. DM or IFG

2. HT (BP ≥ 140/90mmHg) or treated with anti-HT agents

3. Chronic kidney disease (I-IV)

4. Dyslipidemia

5. Smoking

6. Male > 55 , female > 65 years

7. Family history of premature atherosclerosis

Population

Exclusion criteria

1. Patients with acute atherosclerotic disease within 3 months
2. Patients participate in clinical study with blinded intervention
3. Patients with less than 3 years life expectancy (cancer, HIV infection)
4. Patients with large aortic aneurysm require surgical treatment
5. Patients who are not able to follow up

Study protocol

Time	0	6±1	12±1	24±2	36±2	48±2	60±2
(months)							
Visit	1st	2nd	3rd	4th	5th	6th	7th
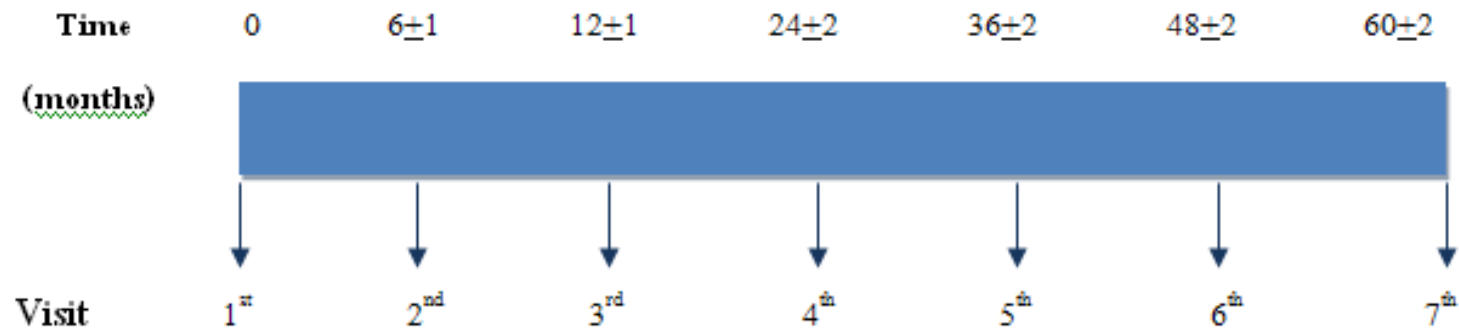
Visit 1

- Inform consent

Each visit :
- History of cardiovascular event
- Physical Examination : Body weight, Waist circumference, Blood pressure and Heart rate
- Laboratory : HbA1C (Fasting blood sugar, Random blood sugar), Lipid profile, Creatinine, CAVI, ECG,ABI
- Treatment: medication, intervention

Planned recruitment:
10000 patients
26 hospitals
100-500 patients/site
Consecutive case
Competitive enrollment

Current status:
**Recruited patients: 9415**
Verified data: 7836

Study sites

- 26 hospitals
- Facility
  - Cath lab: 20 hospitals
  - CVT: 20 hospitals
  - Echocardiogram: 16 hospitals
  - Carotid US: 15 hospitals
- Cardiologist: 23
- Neurologist: 2
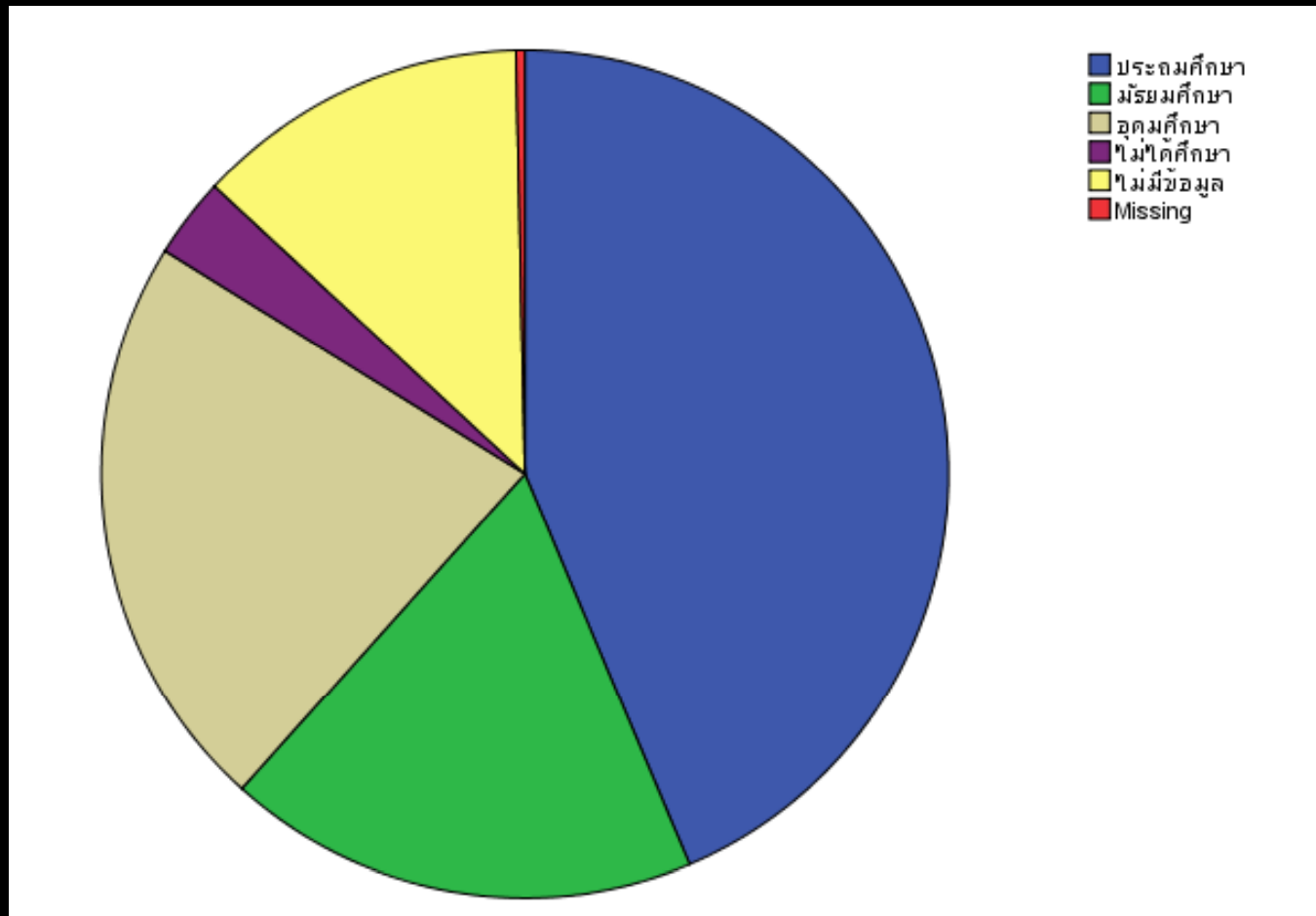- Endocrinologist: 2
- Nephrologist: 4
- Vascular surgeon: 1

Preliminary result:
Baseline characteristics

Health Care Scheme

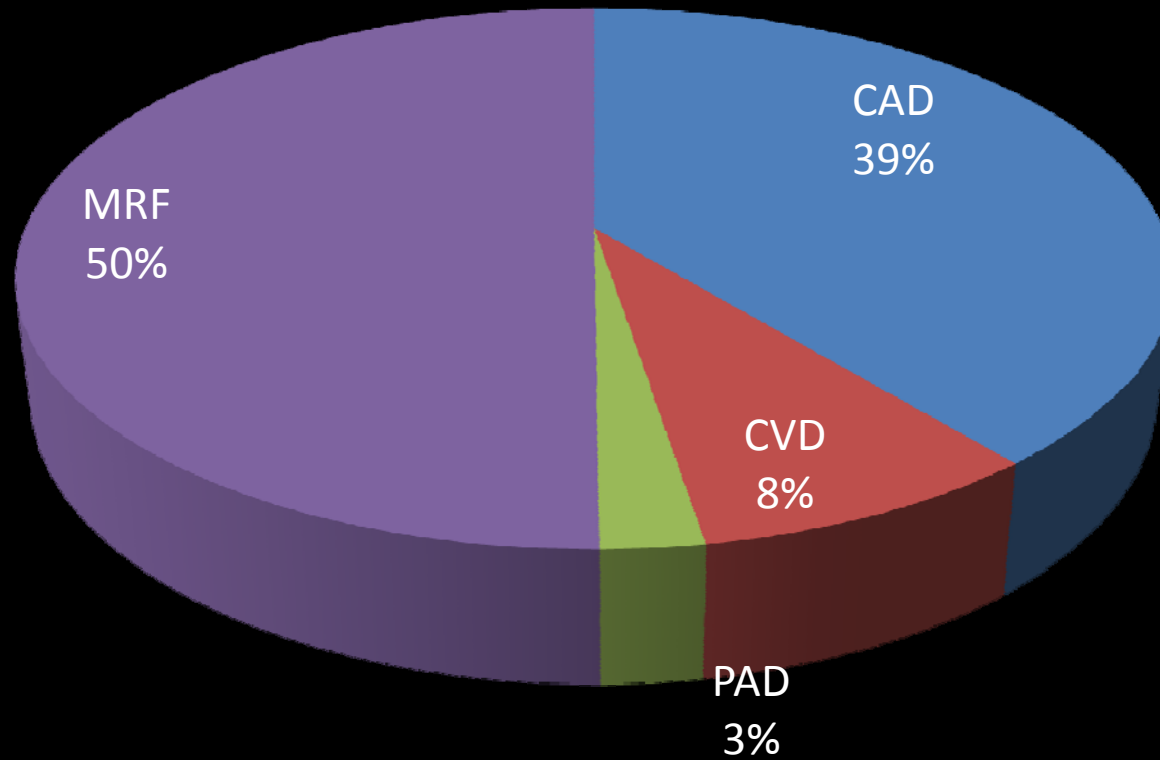■ UHCS   ■ SCC   ■ CSMBS   ■ Private health insurance   ■ Self pay
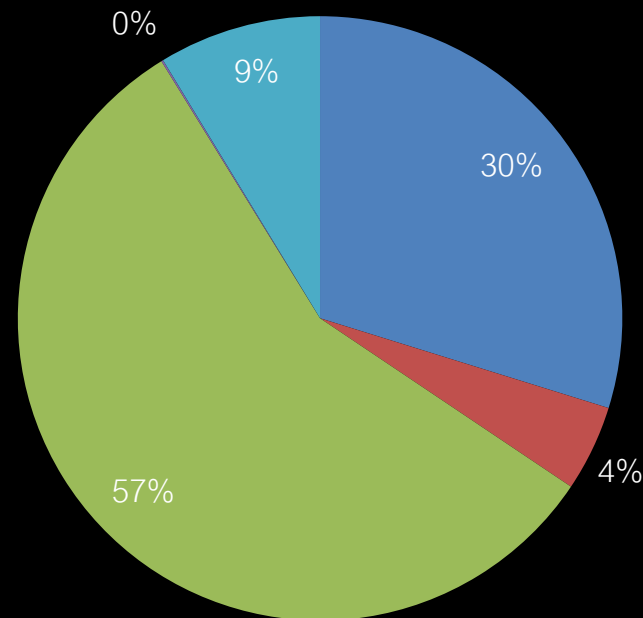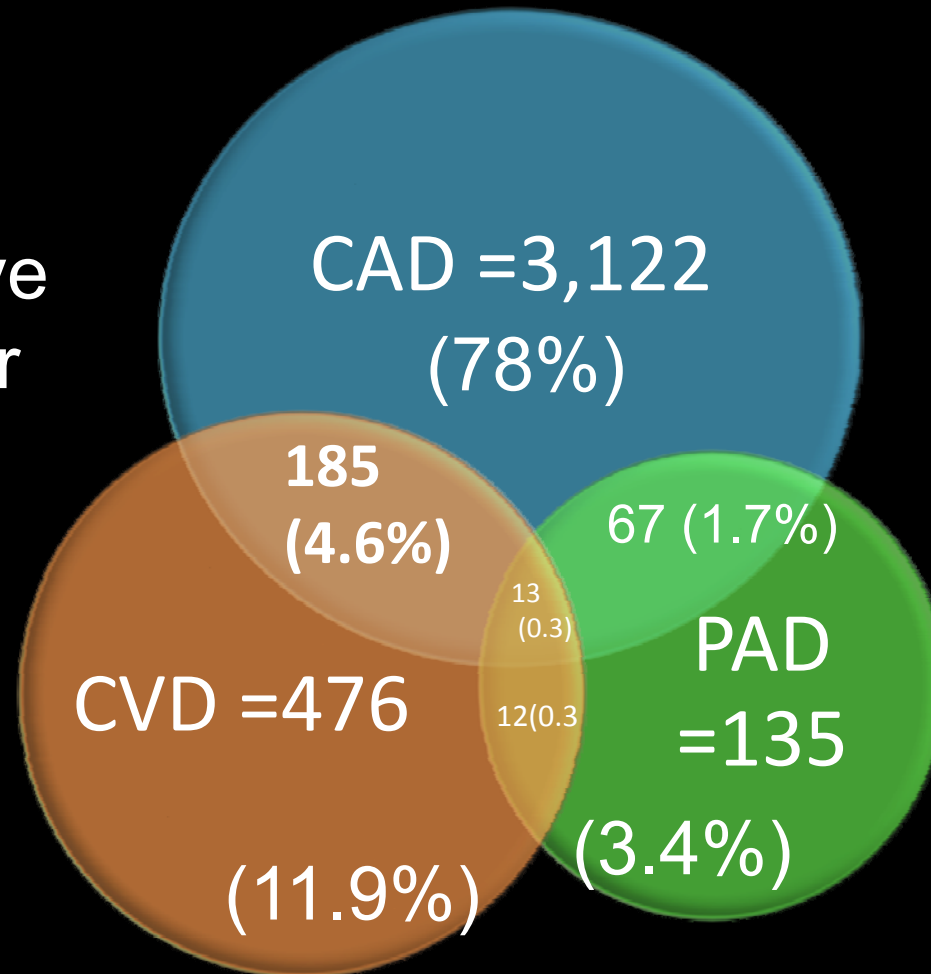
Education level

Patients' inclusion criteria

Proportion of patients according to inclusion criteria

Established atherosclerotic disease

6.9% of patients have polyvascular disease

CAD =3,122 (78%)

185 (4.6%)

67 (1.7%)

13 (0.3)

PAD =135 (3.4%)

CVD =476 (11.9%)

12(0.3

Baseline and index event characteristics

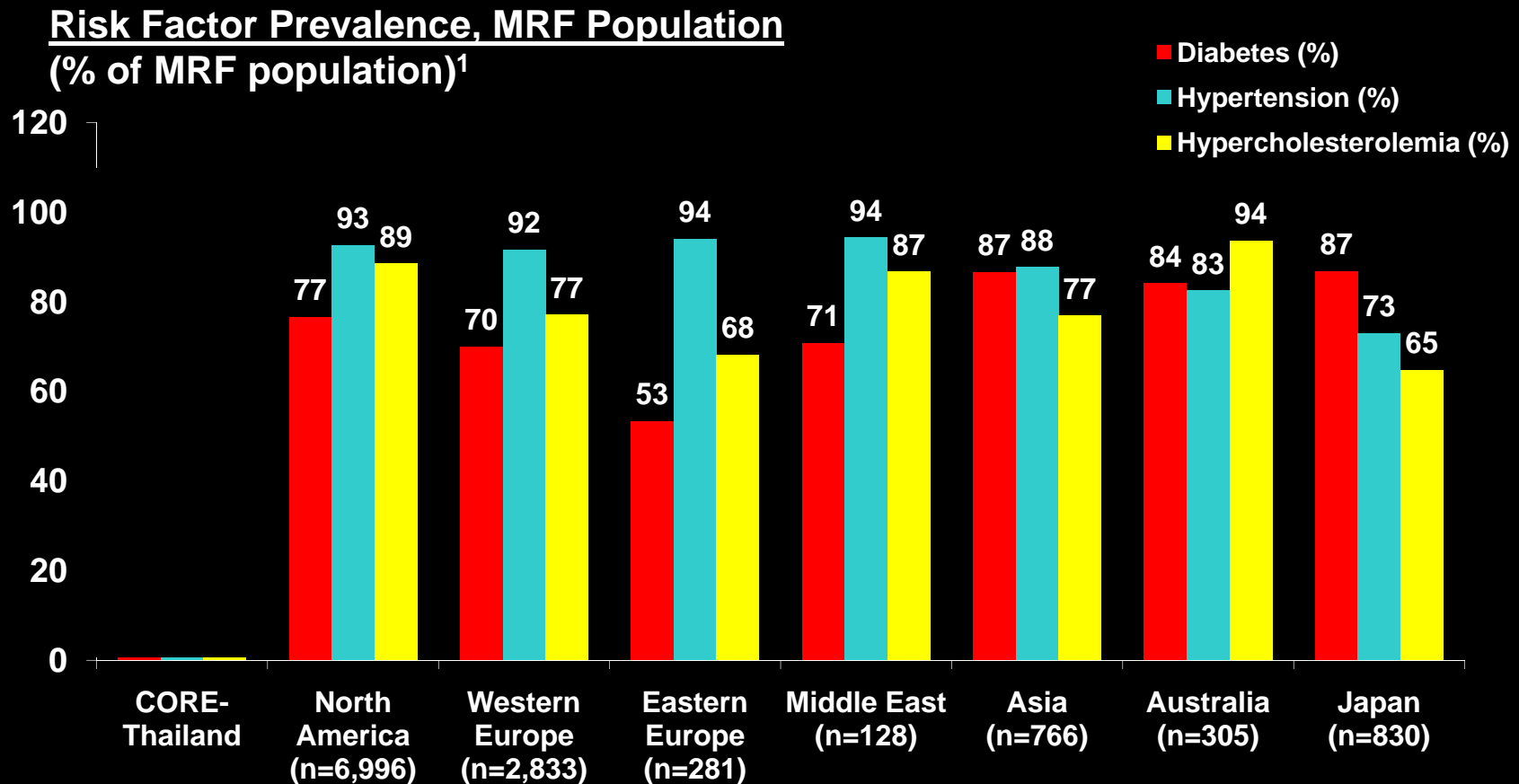|	Total (N=7836)	CAD (3122)	CVD (476)	PAD (135)	Poly Vascular (277)	MRFs (3826)
Age (y)	65 $\pm$10	65 $\pm$10	65 $\pm$10	69 $\pm$11	68 $\pm$10	65$\pm$ 9
Male (%)	53.7	68.1	54.3	53.3	63.3	41.2
BMI	25.4$\pm$4.4	24.9$\pm$4.1	24.4$\pm$4.5	21.9$\pm$5.2	24.3 $\pm$3.9	26.1$\pm$4.5
WC (cm)	88.3$\pm$9.0	87.8$\pm$11	86.2$\pm$11	83.2$\pm$12	86.8 $\pm$11	89.4$\pm$11

All P value < 0.001

Baseline and index event characteristics

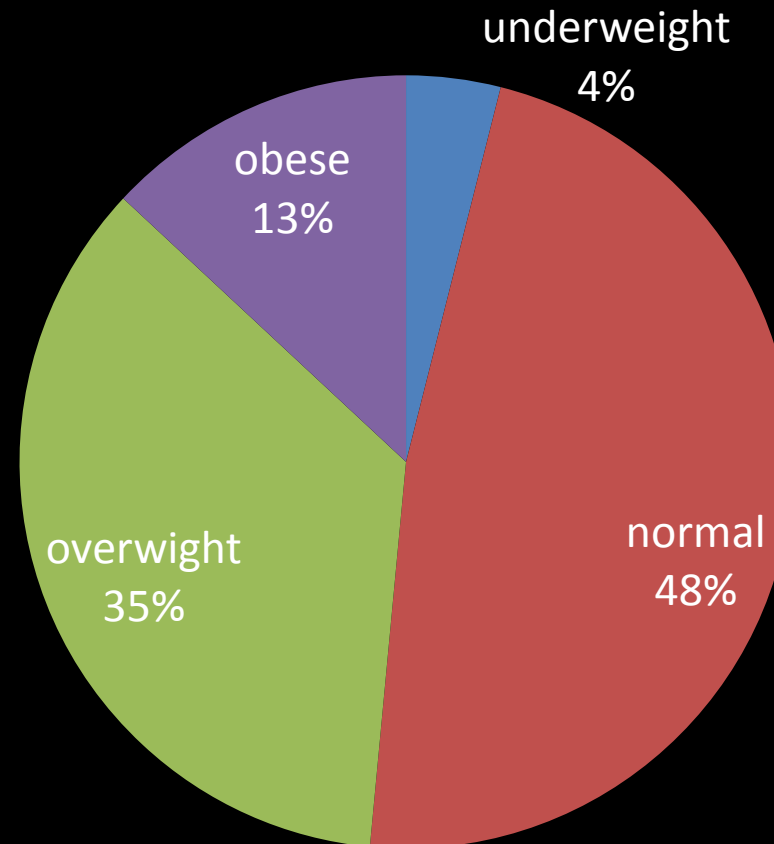|	Total (N=7836)	CAD (3122)	CVD (476)	PAD (135)	Poly Vascular (277)	MRFs (3826)
HT (%)	84.0	73.2	79.8	71.1	87.4	93.7
DM (%)	58.9	41.5	43.3	31.9	47.7	76.8
DLP (%)	86.1	77.7	84.7	67.4	87.4	93.7
Current smoking (%)	5.6	6.9	5.7	12.6	5.7	4.2

All P value < 0.001

Cardiovascular Risk factors within the Multiple Risk Factor group: CORE vs. REACH Registry

Risk Factor Prevalence, MRF Population (% of MRF population)[1]

Legend:
- Diabetes (%)
- Hypertension (%)
- Hypercholesterolemia (%)

Region	Diabetes (%)	Hypertension (%)	Hypercholesterolemia (%)
CORE-Thailand			
North America (n=6,996)	77	93	89
Western Europe (n=2,833)	70	92	77
Eastern Europe (n=281)	53	94	68
Middle East (n=128)	71	94	87
Asia (n=766)	87	88	77
Australia (n=305)	84	83	94
Japan (n=830)	87	73	65

1. Bhatt DL et al, on behalf of the REACH Registry Investigators.
JAMA 2006; 295(2): 180-189.

Undiagnosed disease and risk factors

Undiagnosed PAD
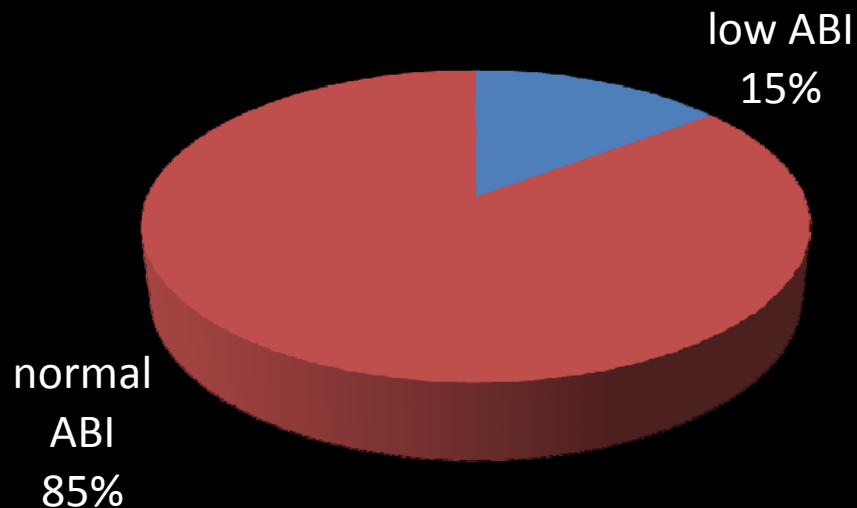
low ABI
15%

15% of undiagnosed
PAD had low ABI

normal
ABI
85%

**Undiagnosed DM
(with HbA1C,n= 245)** ≥ 6.5
19%

< 6.5
81%
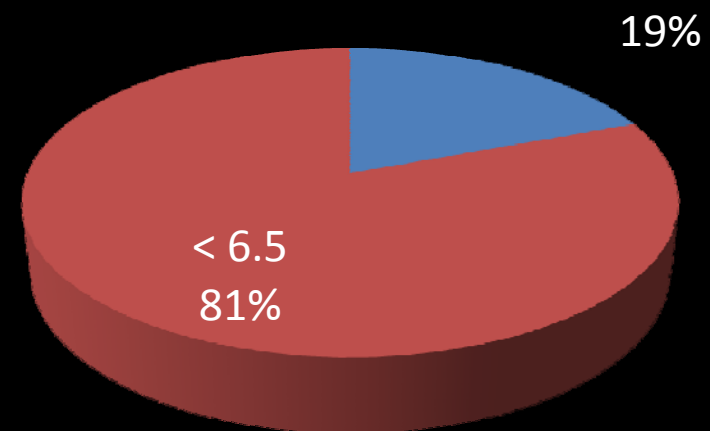
19% of non-diabetic
patients had high HbA_1C

Medications

| Medications	Total N=7836	CAD (3122)	CVD (476)	PAD (135)	Polyvascular (277)	Risk factors (3826)
Antiplatelets	72.2	98.2	92.2	81.5	96.4	46.5
Aspirin	45.5	50.3	56.9	45.2	41.2	40.4
Clopidogrel	2.9	3.5	10.3	3.0	6.9	1.2
Aspirin + clopidogrel	17.6	39.8	1.9	6.7	28.5	1.1
Statin	87.8	95.0	80.0	65.2	90.6	83.4
Fibrate	8.0	5.8	5.6	3.8	4.8	10.3

All P value < 0.001

Antihypertensive agents in HT patients

| Medications	Total N=6586	CAD (2284)	CVD (379)	PAD (96)	Polyvascular (242)	Risk factors (3582)
Antihypertensive agents	96.9	99.2	90.8	83.3	94.6	96.7
Beta blocker	53.7	82.0	36.1	56.3	72.7	36.3
CCB	45.9	35.4	45.8	42.7	37.2	53.3
ACEI	35.4	40.9	30.8	16.7	35.1	33.0
ARB	36.5	33.3	30.8	11.5	25.2	40.6
Diuretics	30.5	27.2	25.3	30.2	36.8	32.8

All P value < 0.001

Number of anti-diabetic agents in DM patients

- 1 — 33%
- 0 — 21%
- 2 — 32%
- 3 — 13%
- 4 — 1%
- 5 — 0%
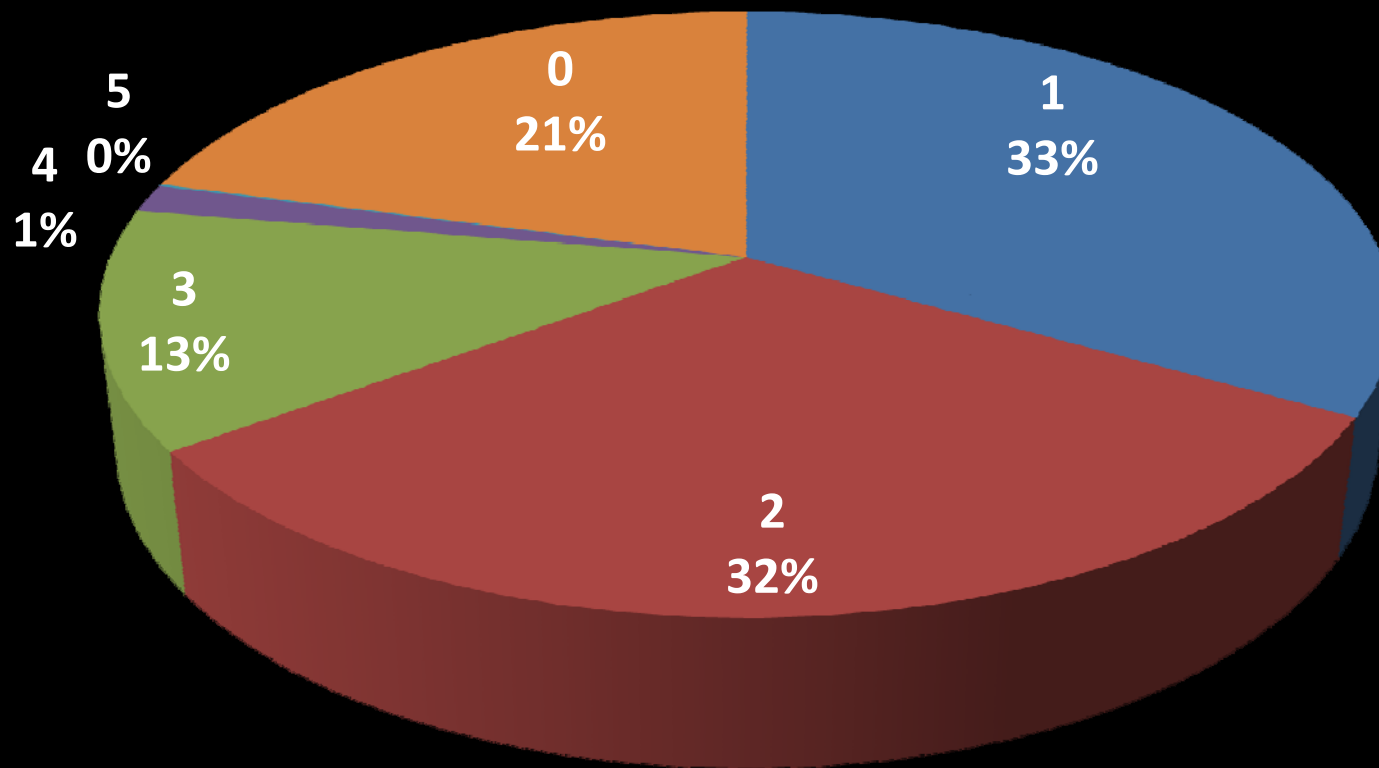
46% of DM patients received ≥ 2 anti-diabetic agents
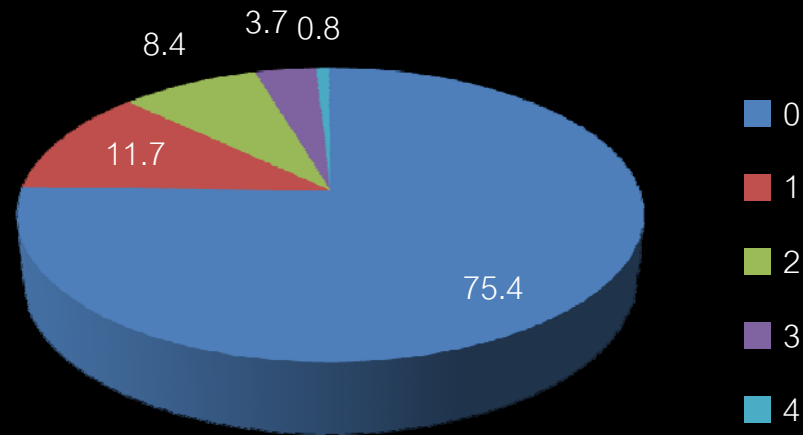
Anti-diabetic agents (N= 3870)
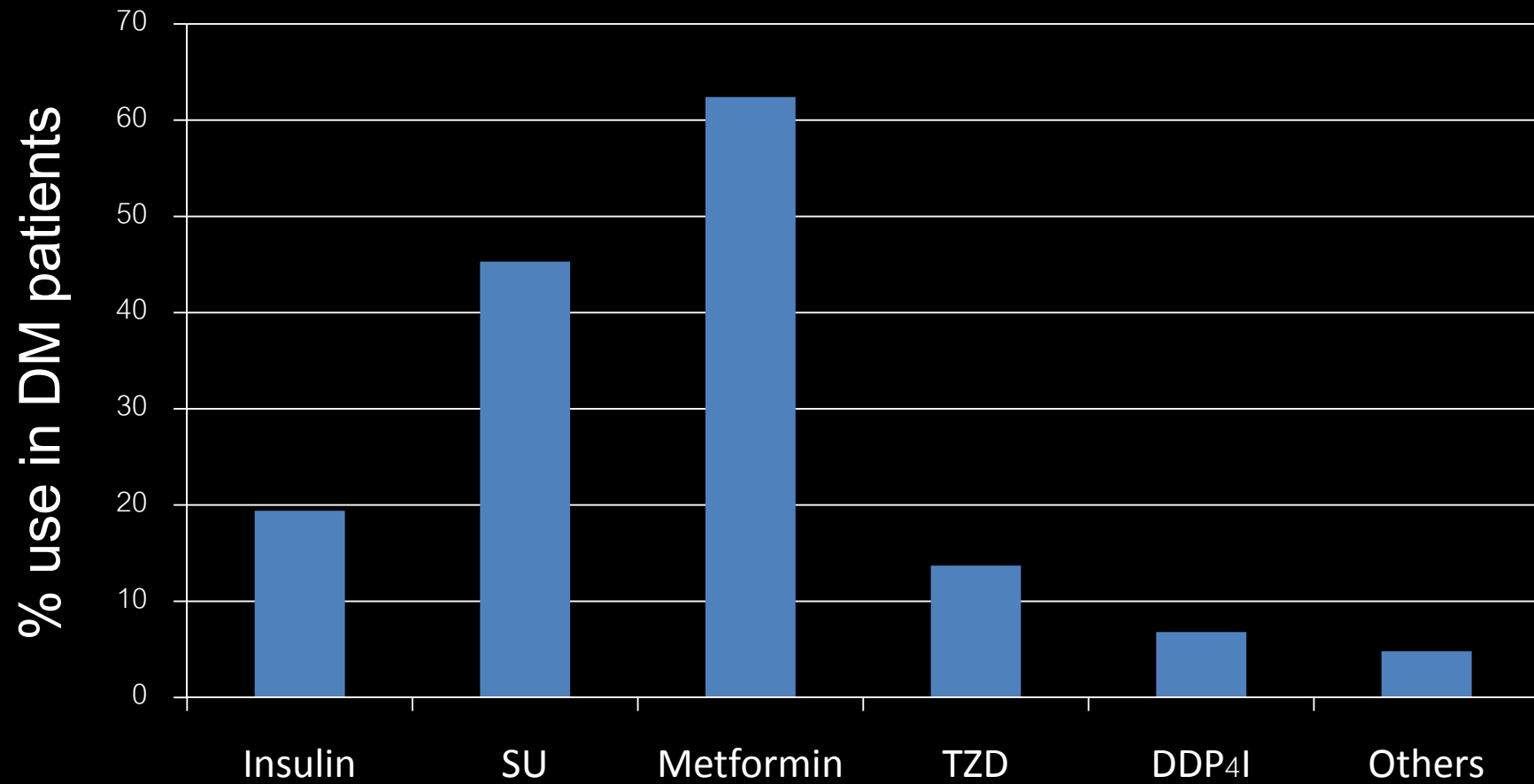
Medications in diabetic patients

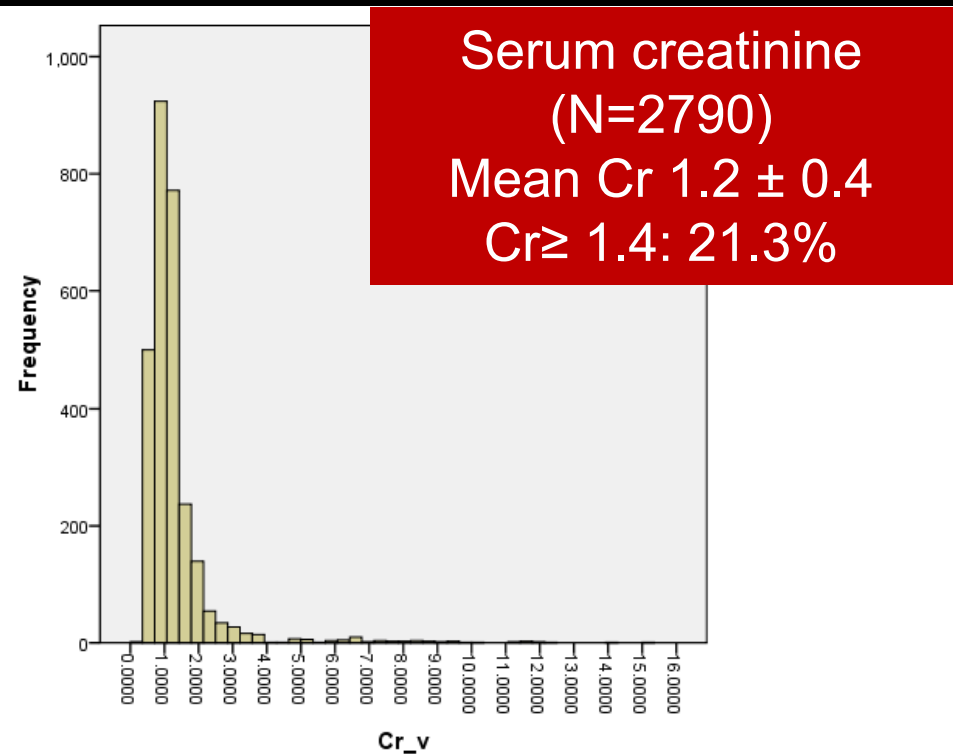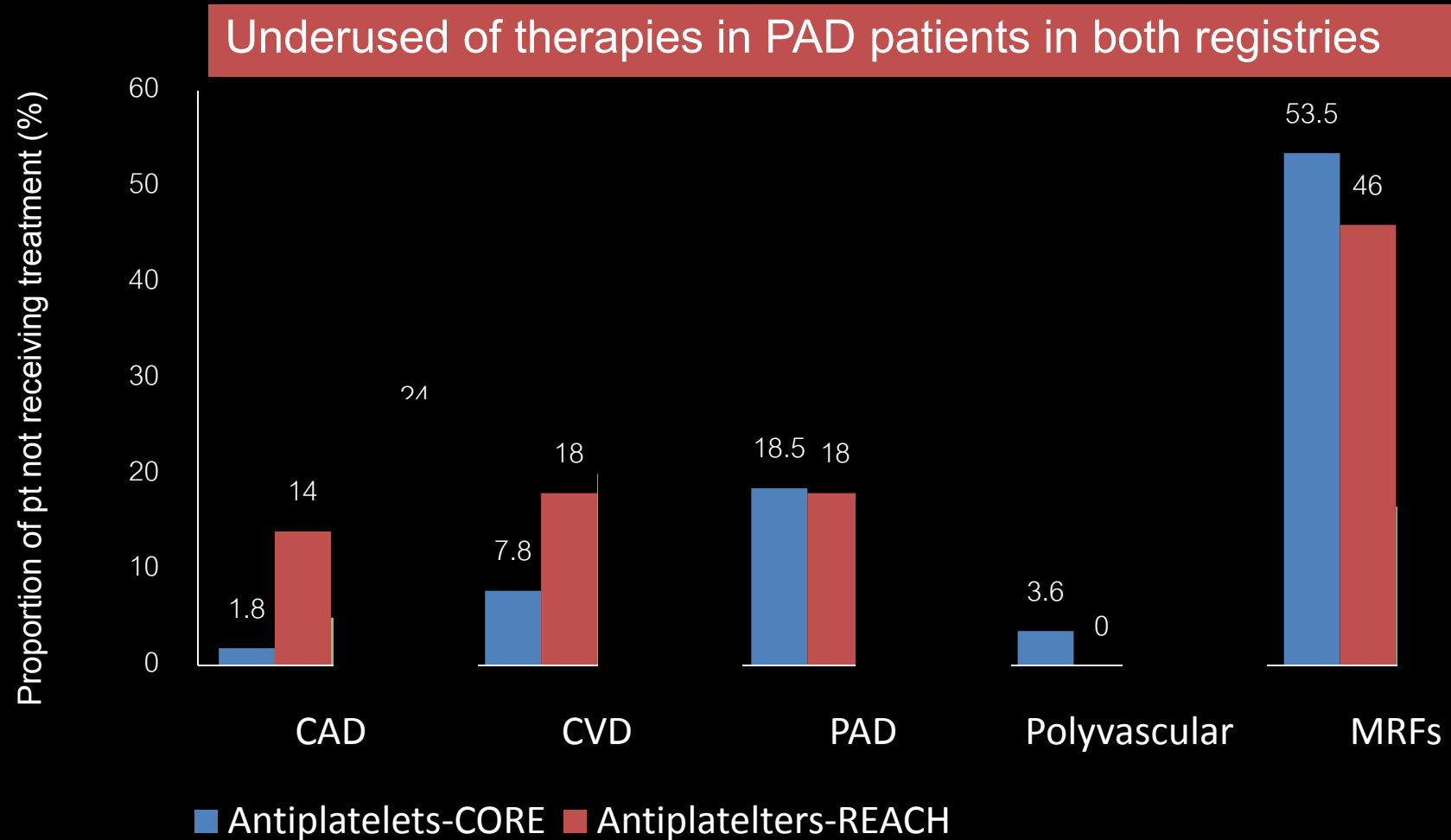| Medications	Total N=4617	CAD (1297)	CVD (206)	PAD (43)	Polyvascular (132)	Risk factors (2939)
Antidiabetic agents	80	79.6	66.7	46.3	74.3	81.8
Sulfonylurea	*43.5*	*45.2*	*32.0*	*22.0*	*41.9*	*44.0*
Metformin	*60.9*	*57.7*	*45.7*	*17.1*	*42.9*	*64.5*
Insulin	*17.6*	*14.6*	*11.0*	*17.1*	*19.0*	*19.4*
Statin	81.2	95.1	82.2	61.0	91.4	84.5
ACEi	34.7	38.3	31.5	12.2	36.2	33.8
ARB	37.0	33.6	31.1	22.0	23.8	39.5
Aspirin	60.8	92.8	63.9	70.7	81.9	46.4

All P value < 0.001

DM and renal

Urine protein (n=1211)

Legend: 0, 1, 2, 3, 4

Values: 75.4, 11.7, 8.4, 3.7, 0.8

**Serum creatinine (N=2790)
Mean Cr 1.2 ± 0.4
Cr≥ 1.4: 21.3%**

21% of DM patients had sCr > 1.4 mg/dL

Underused of established therapies

Underused of therapies in PAD patients in both registries

Proportion of pt not receiving treatment (%)

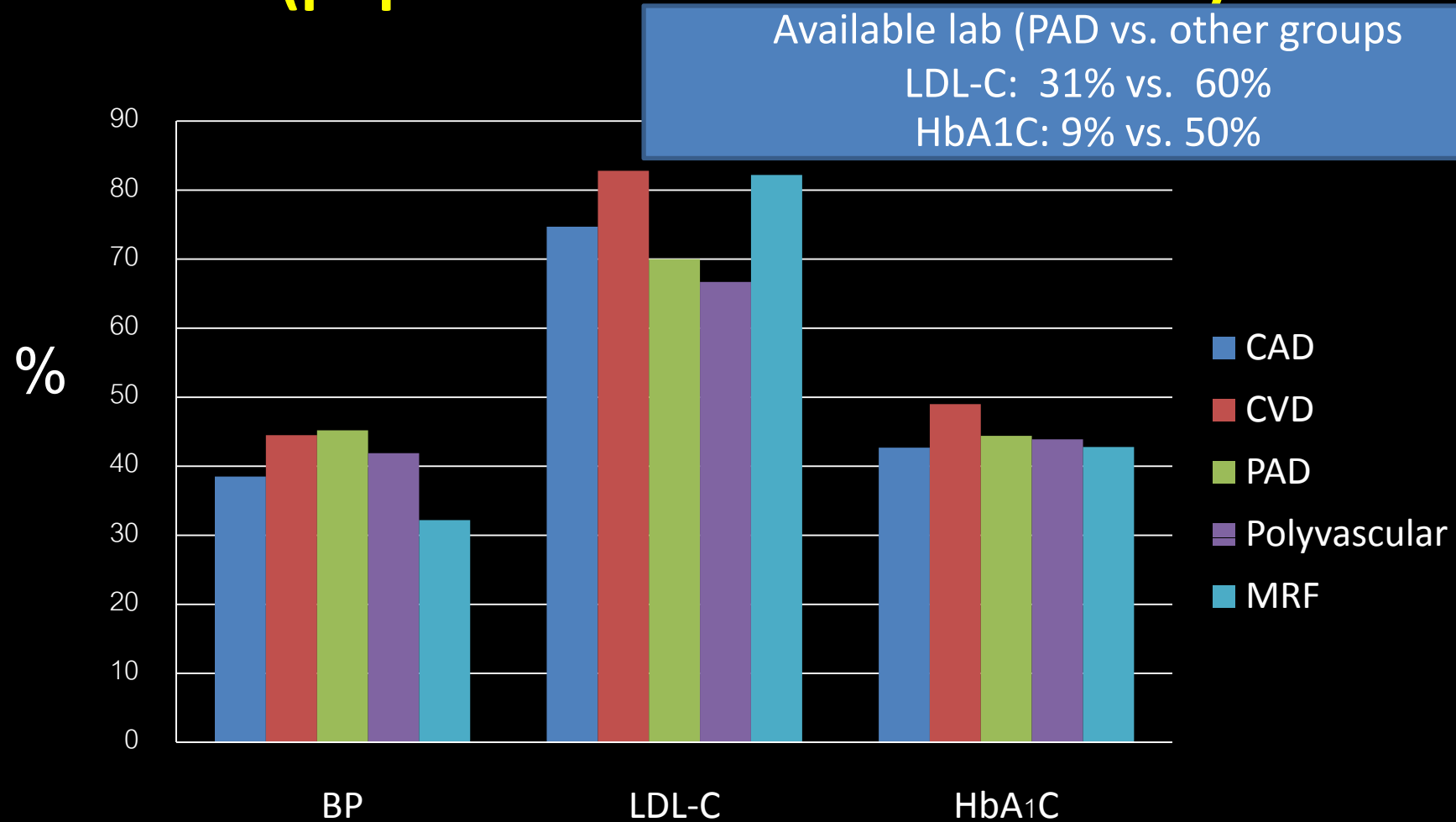| Category	Antiplatelets-CORE	Antiplatelters-REACH
CAD	1.8	14
CVD	7.8	18
PAD	18.5	18
Polyvascular	3.6	0
MRFs	53.5	46

- Antiplatelets-CORE
- Antiplatelters-REACH

Baseline and index event characteristics

Characteristic	Total N=7836	CAD (3122)	CVD (476)	PAD (135)	Poly vascular (277)	MRFs (3826)
SBP (mmHg)	132$\pm$19	129$\pm$19	132$\pm$29	132$\pm$23	130$\pm$23	134$\pm$16
DBP (mmHg)	74$\pm$15	74$\pm$11	76$\pm$12	72$\pm$12	74$\pm$12	75$\pm$11
LDL-C (mg/dl)	94$\pm$36	91$\pm$35	90$\pm$30	89$\pm$40	90$\pm$40	97$\pm$36
HDL-C (mg/dl)	50$\pm$14	46$\pm$13	50$\pm$18	45$\pm$15	45$\pm$13	53$\pm$15
TG (mg/dL)	141$\pm$92	145$\pm$83	131$\pm$82	142$\pm$78	144$\pm$80	139$\pm$88

All P value < 0.05

Uncontrolled risk factors
(population with available data)

Available lab (PAD vs. other groups
LDL-C: 31% vs. 60%
HbA1C: 9% vs. 50%

%

- CAD
- CVD
- PAD
- Polyvascular
- MRF

BP   LDL-C   HbA1C

BP < 140/90mmHg
LDL-C < 70 in established disease, < 100 in MRFs
HbA1C < 7%

Healthcare scheme and risk factor control

|	UHCS (N =1600)	SSS (N =184)	CSMBS (N = 1995)	Others (N =230)	P value
LDL < 70mg/dL	10.6%	10.3%	14.0%	12.6%	0.014
HbA1C < 7%	11.4%	16.8%	19.0%	17.8%	< 0.001
BP < 140/90mmHg	69.8%	67.9%	67.8%	65.7%	0.461
All 3 RFs	1.6%	2.7%	3.2%	2.6%	0.028

Disease categories and 6 months event rate (N= 4443)

Major adverse cardiovascular event:
death or nonfatal MI or nonfatal stroke

	Death/MI/stroke	Death/MI/UA/ stroke/TIA/HF
CAD	1.2	2.7
CVD	1.6	1.6
PAD	5.9	17.6
Polyvascular	1.7	2.6
MRFs	0.4	0.6
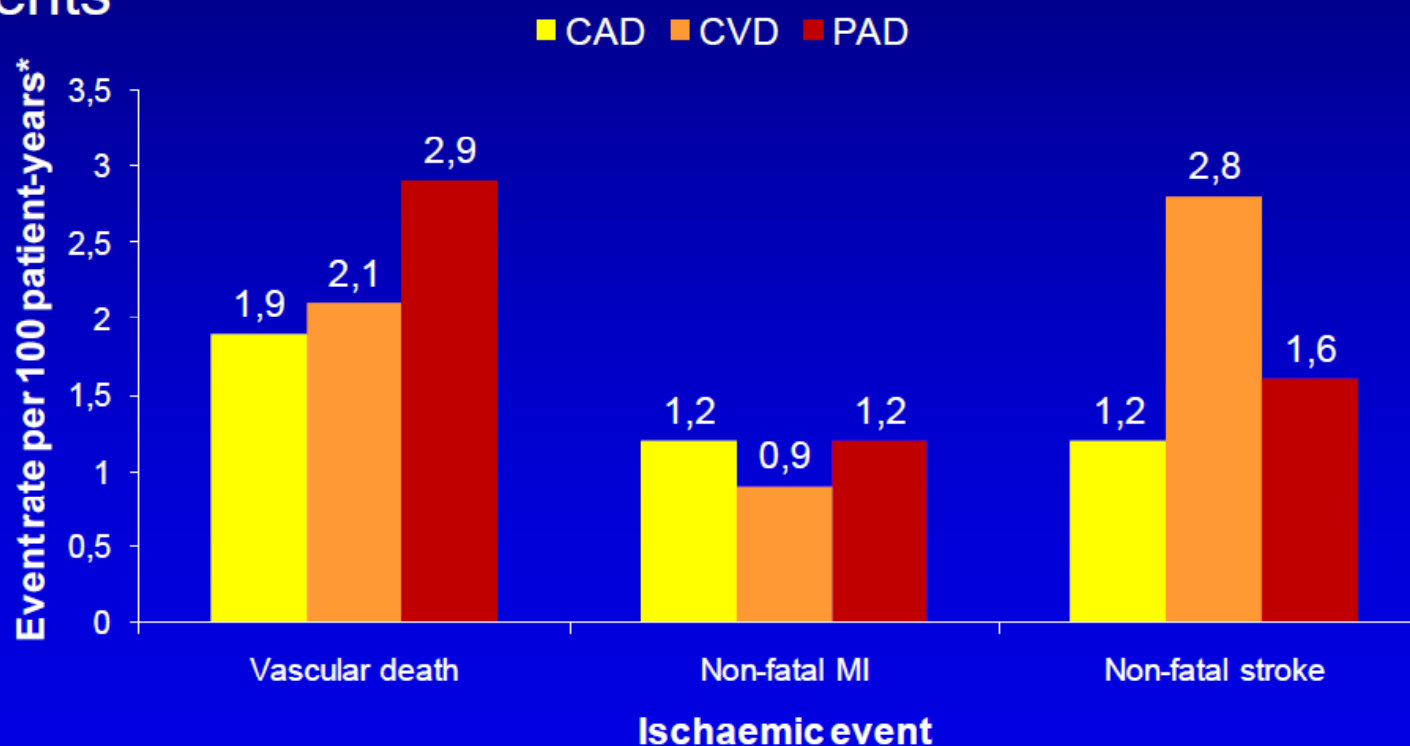
Health Care Scheme and 6 months MACE (N= 4443)

	Death/MI/stroke	Death/MI/UA/ stroke/TIA/HF
UHCS	1.1	2.3
SSC	0.5	1.0
CSMBS	0.6	1.3
Others	1.1	1.6

Information from baseline characteristics: CORE

- 94% of planned recruitment
- High proportion of CAD and MRF groups
- High prevalence of classic atherosclerotic risk factors
- High rate of antiplatelet and statin use for secondary prevention
- High rate of uncontrolled risk factors
- Benefit of risk factors control in real life practice

What are we doing now?

- Complete recruitment

- Complete data analysis for baseline characteristics

- Manuscript preparation for baseline characteristic and prevalence of atheroslcerotic risk factors

- Follow up visits

CORE-Extended study

- CORE-Metabolic syndrome

  - Metabolic syndrome and CV risk

  - Bone fracture in metabolic syndrome

  - Cognitive function in metabolic syndrome

- CORE substudy

  - CORE-platelet reactivity

  - CORE-biomarkers: hsCRP, soluble ST2

What will we get from the CORE-Thailand

With long term (≥5 years of clinical follow-up)

CORE- Thailand will

- provide intermediate and long-term data of real-world event rates, treatment patterns and outcomes

- help to improve assessment and management of stroke, heart attack and associated risk factors

- provide data of cost-effectiveness of risk factor control

Acknowledgement

- สำนักงานคณะกรรมการวิจัยแห่งชาติ

- เครือข่ายวิจัยกลุ่มสถาบันแพทยศาสตร์แห่งประเทศไทย

- สมาคมโรคหัวใจแห่งประเทศไทย

- สมาคมโรคหัวใจแห่งประเทศไทย

  - **Sanofi Aventis**

  - **Astra Zenaca**

Acknowledgement

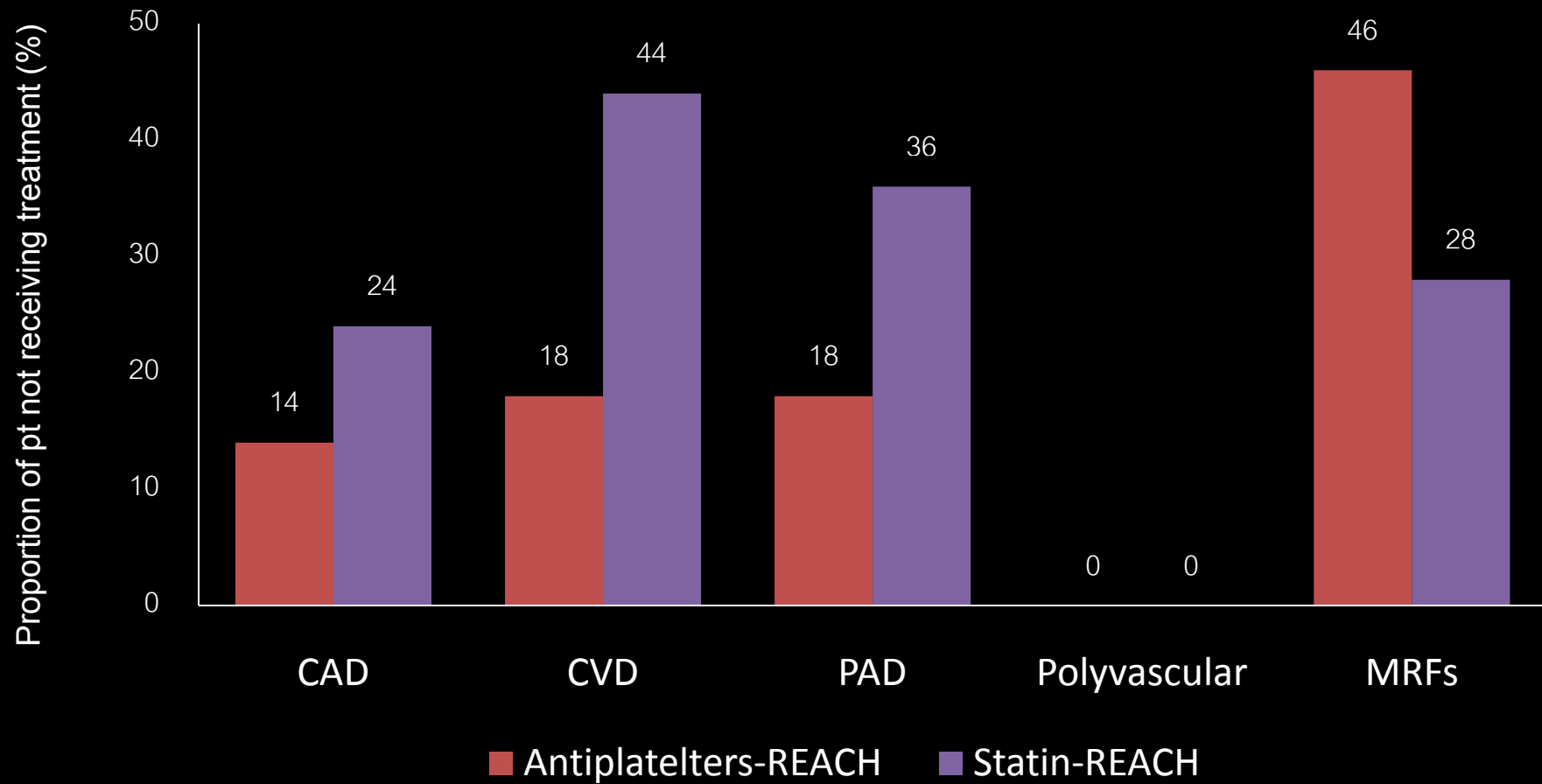Prof. Pyatas Tasanawiwat

Prof. Piyamitr Sritara

Prof. Rungroj Kritayapong

Assist. Prof. Smonporn Boonyaratvej Srisongmeung

Dr. Sukit Yamwong

Assist. Prof. Rapeephon Kunjara -Na –Ayudhya

Underused of established therapies in REACH registry

Proposed research questions

- Baseline characteristics of high atherosclerotic risk patients in Thailand

- Risk factors control and factors determine the guideline containment of risk factor control in different populations (CAD vs. CVD vs. PAD vs. MRF)

Proposed research questions

- The association of hs-CRP level and cardiovascular events

- The association of arterial stiffness/ ankle brachial index and cardiovascular events

- The association of arterial stiffness/ ankle brachial index and cerebrovascular events

- The association of renal insufficiency and CV events

- The novel markers of renal injury and CV events

Atherosclerotic risk factors

Conventional risk factors

- Non-modifiable
  - Age
  - Sex
  - Genetics
- Modifiable
  - Smoking
  - Hypertension
  - Dyslipidemia
  - Diabetes
  - Abdominal obesity
  - Physical inactivity

Emerging risk factors /markers

- Inflammatory marker (hsCRP)
- ….
- …

Data management

- MedResNet (CRCN)
  - OMERET system
  - Data management
    - Data clarification
    - Data validation

Current status

- 1st investigator meeting: 19 Nov. 2010
- 2nd Investigator meeting: 2011
- 3rd investigator meeting: 23 March2013

Participating physicians

- Invitation through the Heart Association of Thailand meeting, other society meetings, free media (magazine)

- Physician profile
  :internist, cardiologist, nephrologist, neurologist, endocrinologist, vascular surgeon

Study sites

โรงพยาบาลพระปกเกล้าจันทบุรี

โรงพยาบาลมหาราชนครเชียงใหม่

โรงพยาบาลนครพิงค์

ศูนย์หัวใจสิริกิติ์ มหาวิทยาลัยขอนแก่น

โรงพยาบาลมหาราชนครราชสีมา

มหาวิทยาลัยเทคโนโลยีสุรนารี

โรงพยาบาล พระมงกุฎเกล้า

โรงพยาบาลธรรมศาสตร์

Study sites

โรงพยาบาลราชวิถี

สถาบันทรวงอก

ศูนย์การแพทย์สมเด็จพระเทพ ฯ มหาวิทยาลัยศรีนครินทร์วิโรฒ

โรงพยาบาลมหาวิทยาลัยบูรพา

โรงพยาบาลศิริราช

โรงพยาบาลรามาธิบดี

โรงพยาบาลวชิรพยาบาล

โรงพยาบาลชลบุรี

โรงพยาบาลจุฬาลงกรณ์

Study sites

โรงพยาบาลตำรวจ

โรงพยาบาลเชียงรายประชานุเคราะห์

โรงพยาบาลแพร่

โรงพยาบาลลำปาง

โรงพยาบาลมหาวิทยาลัยนเรศวร

โรงพยาบาลราชเวช

โรงพยาบาลศูนย์ขอนแก่น

โรงพยาบาลสงขลานครินทร์

ศูนย์การแพทย์กาญจนาภิเษก

Preliminary analysis:
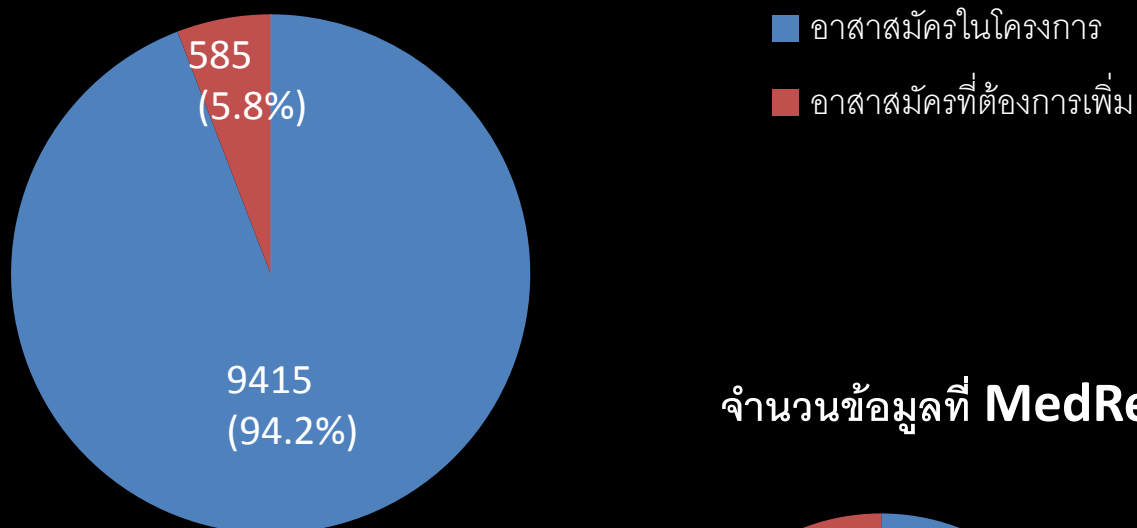# Baseline characteristics analysis

Objective

- To determine the atherosclerosis risk factor prevalence and treatment

Data collection

- Demographic data
- Inclusion criteria (risk factors, established atherosclerotic disease)
- Physical examinations
- Investigations
- Treatment (medications and interventions)
- New cardiovascular events