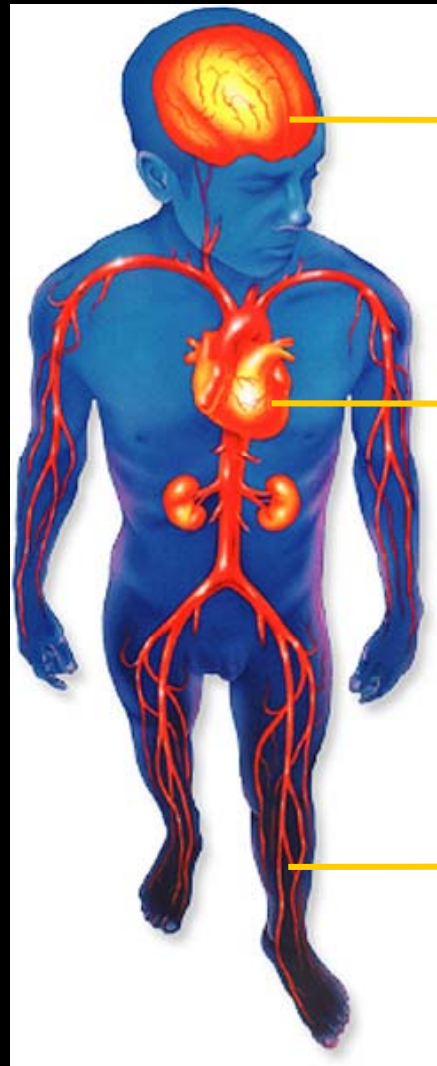# A cohort of patients with high risk for cardiovascular events (CORE-Thailand) : Baseline characteristics

Arintaya Phrommintikul, M.D.

on behalf of the investigators

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.

Atherosclerotic risk factors

Conventional risk factors

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

Emerging risk factors

- Inflammatory marker (hsCRP)
- ….
- …

Limitation of the current information

- 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 Thai high atherosclerotic risk patients

CORE-Thailand: Objectives

Secondary objectives

- To study the atherosclerotic risk factors/risk factor control in Thai population

- To evaluate "current" risk score in predicting cardiovascular events and develop appropriate predictive risk score

- To study "real world" practice in treatment of atherosclerotic patients among various level of hospitals

Study design

- Prospective cohort study

- Population: Patients with high atherosclerotic risk who have been treated in the hospitals

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

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

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 (type I or 2) 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

Data collection

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

Study protocol

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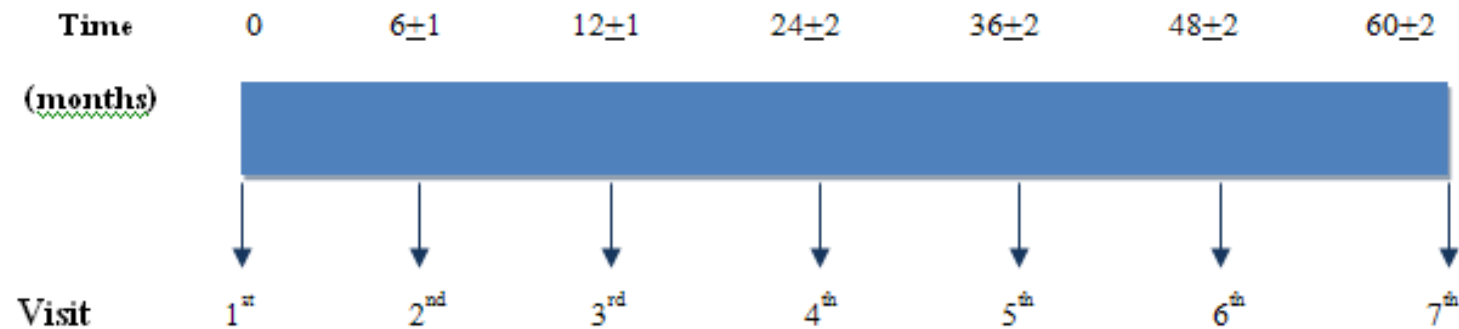
Visit 1

- 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

Data management

- MedResNet (CRCN)
  - OMERET system
  - Data management will be performed by MedRestNet
    - Data clarification
    - Contact investigator for queries
    - Data validation

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

Current status:
Recruited patients: 7480
Verified data: 6292

Baseline characteristics analysis

Objective

– To determine the atherosclerosis risk factor prevalence and treatment

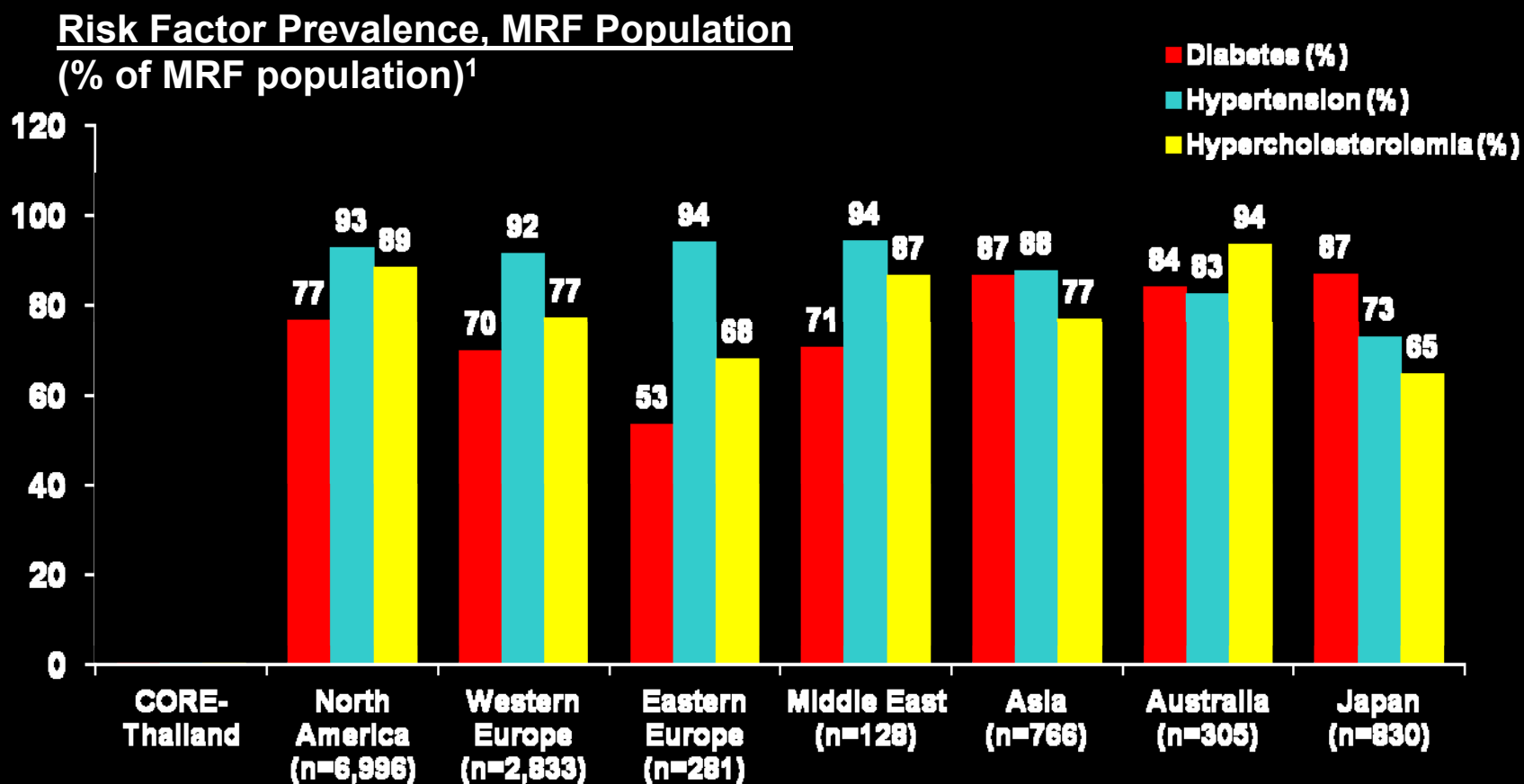# Preliminary results

Baseline and index event characteristics

Characteristic	Total (N= 6292)	CAD (2543)	CVD (443)	PAD (131)	Multiple Risk factors (3355)
Median age, years	65.3(9)	65.1 (10)	66 (10)	69(11)	65(9)
Men, %	53.0	68.5	40.6	51.3	41.5
DM, %	61.5	42.5	52.4	39.7	77.3
HT, %	83.5	71.5	84.9	77.9	93
Dyslipidemia, %	86.4	77.9	88.5	83.2	93
Smoker (current)	5.7	7.2	6.1	10.0	4.6
CKD	19.6	16.5	23.3	31.3	21.5
FHx of premature atherosclerosis	8	7.1	6.8	11.6	8.7

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 (%)

Data values by region:

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%

normal
ABI
85%

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

< 6.5
81%
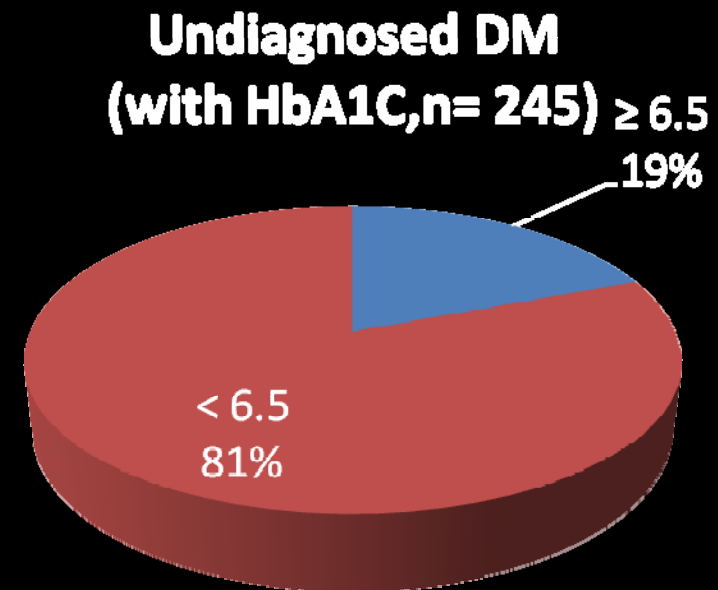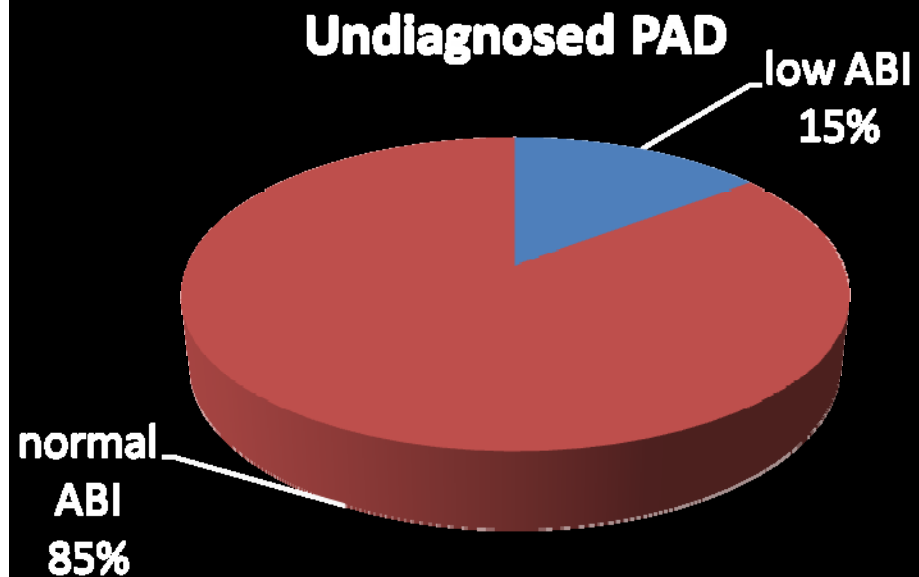
Baseline characteristics of risk factors

Characteristic	Total (N= 6292)	CAD (2543)	CVD (443)	PAD (131)	Risk factors (3355)
Waist circumference(cm)	88(13)	88(11)	88(11)	84(15)	89(11)
SBP (mmHg)	132(18)	130(19)	133(19)	132(22)	134(17)
DBP (mmHg)	74(11)	74(11)	76(12)	71(12)	75(11)
LDL-C (mg/dl)	93(33)	94(32)	94(30)	90(37)	100(34)
HDL-C (mg/dl)	50(15)	46(13)	50(19)	46(16)	52(14)
TG (mg/dL)	142(94)	147(80)	137(87)	141(80)	174(40)
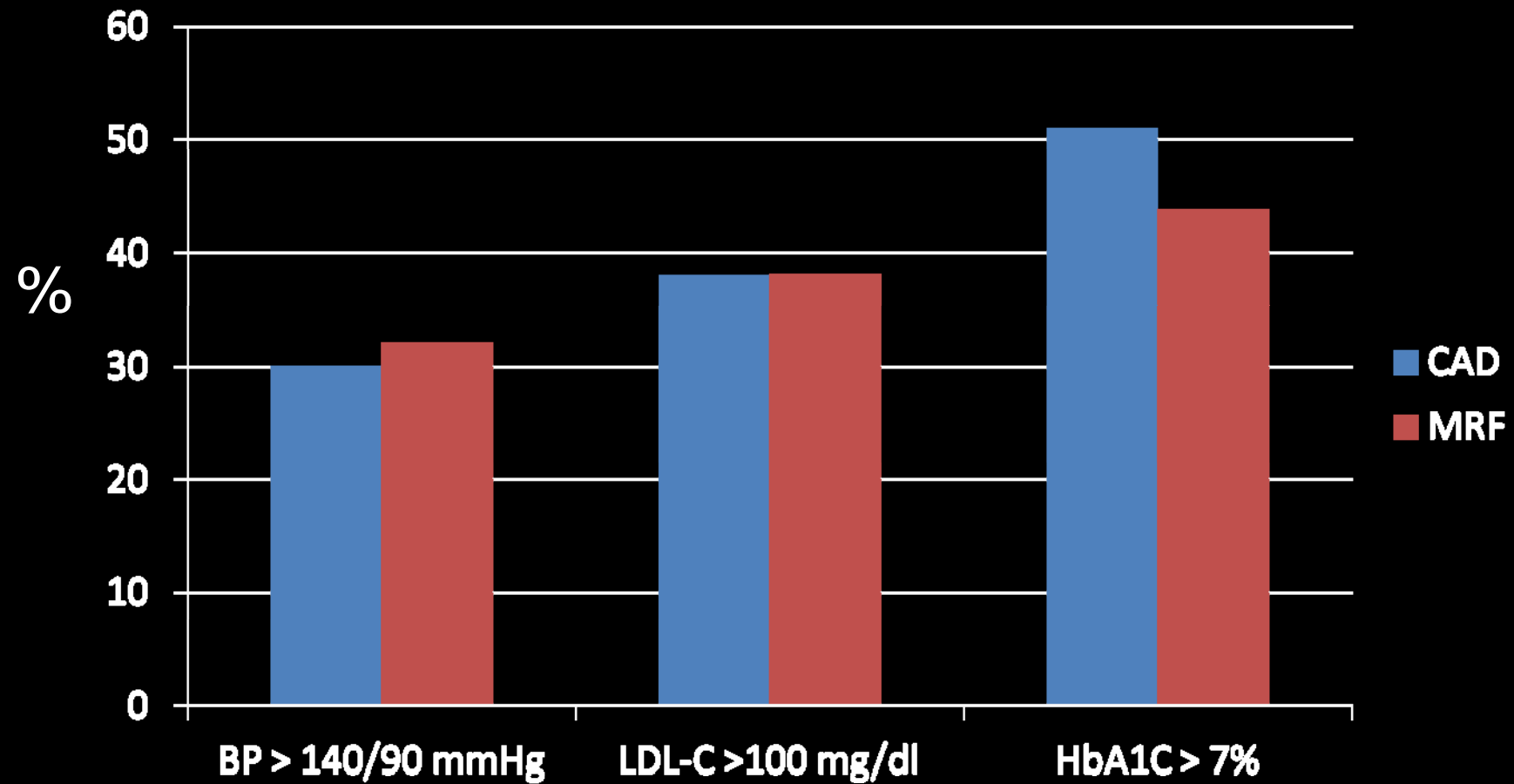
Medications

Medications	Total (N= 6292)	CAD (2543)	CVD (443)	PAD (131)	Risk factors (3355)
Antiplatelet Rx (≥1)	70.6	96.9	94.4	90.1	48.2
Aspirin	65.3	92.8	71.3	76.3	44.1
Clopidogrel	20.8	42.4	21.4	25.3	5.0
Beta blocker	54.5	81.8	49.9	55.0	35.6
CCB	40.4	30.1	38.6	32.1	48.6
ACEI	34.9	39.9	33.9	22.9	32.1
ARB	32.8	28.1	26.2	16.0	37.4
Statin	88.6	95.6	87.1	83.2	84.2

Medications in CAD and MRF groups
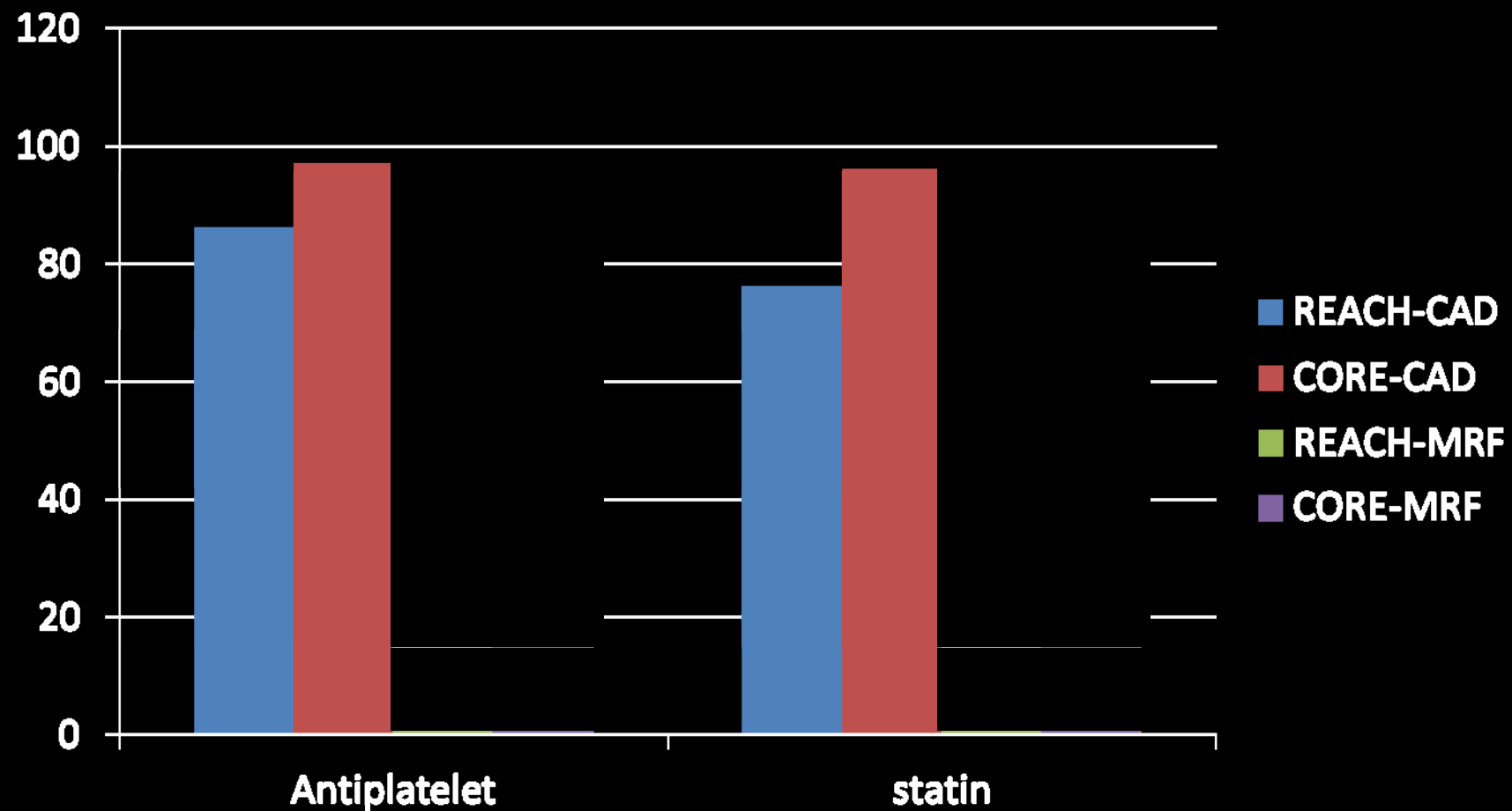
Information from baseline characteristics

- Data from 65% of planned recruitment
- High proportion of CAD and MRF groups
- High prevalence of classic atherosclerotic risk factors and high prevalence of uncontrolled risk factors
- High rate of antiplatelet and statin use for secondary prevention
- High rate of statin use for primary prevention
- Benefit of risk factors control in real life practice

CORE: ongoing

- Complete data on baseline characteristic at recruitment
- Data from 6 months follow up
  - Risk factor control
  - Investigation and intervention
  - Short term cardiovascular event rate

Acknowledgement

Prof. Tada Yipintsoi

Prof. Pyatas Tasanawiwat
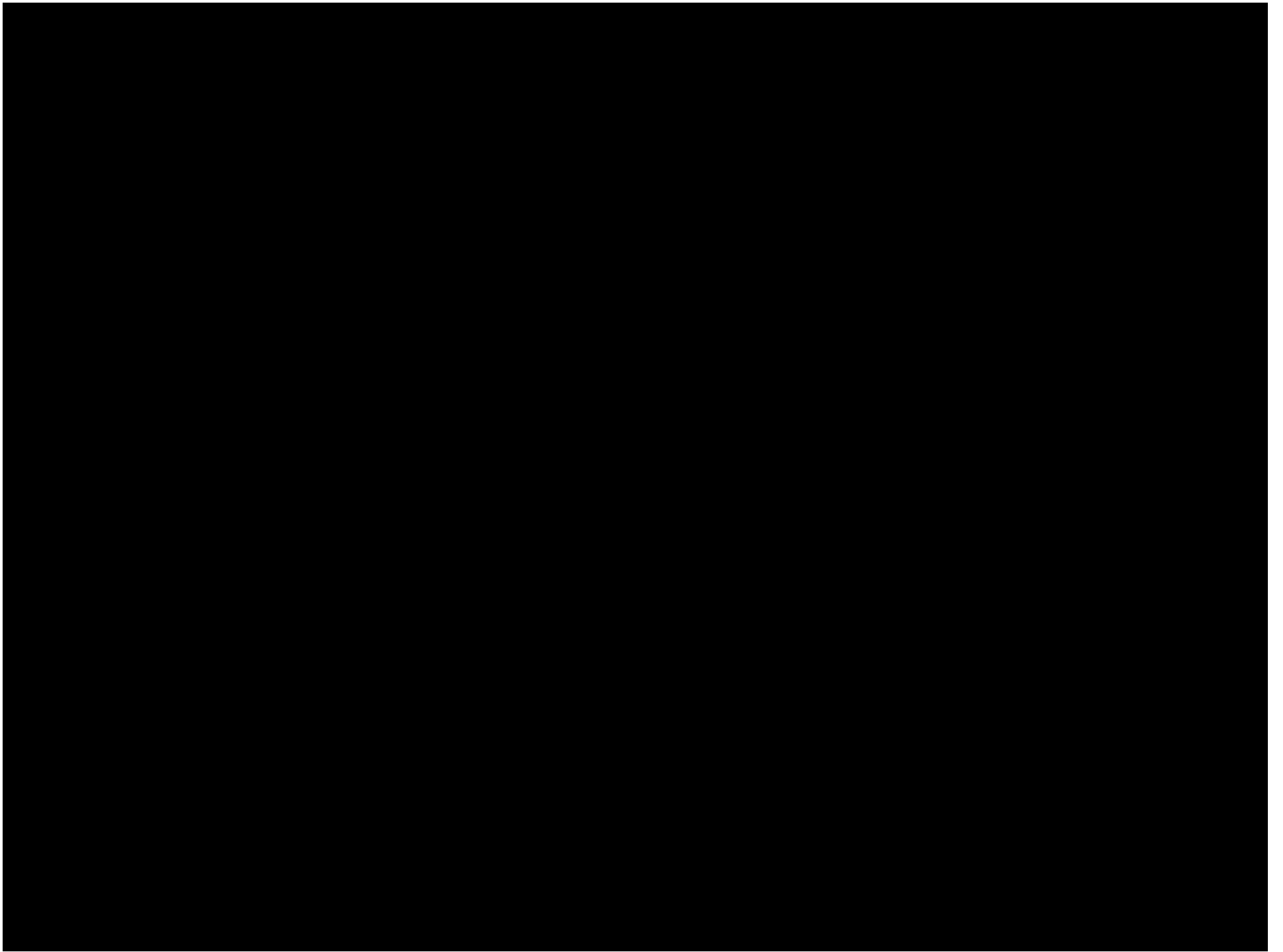
Prof. Piyamitr Sritara

Prof. Rungroj Kritayapong

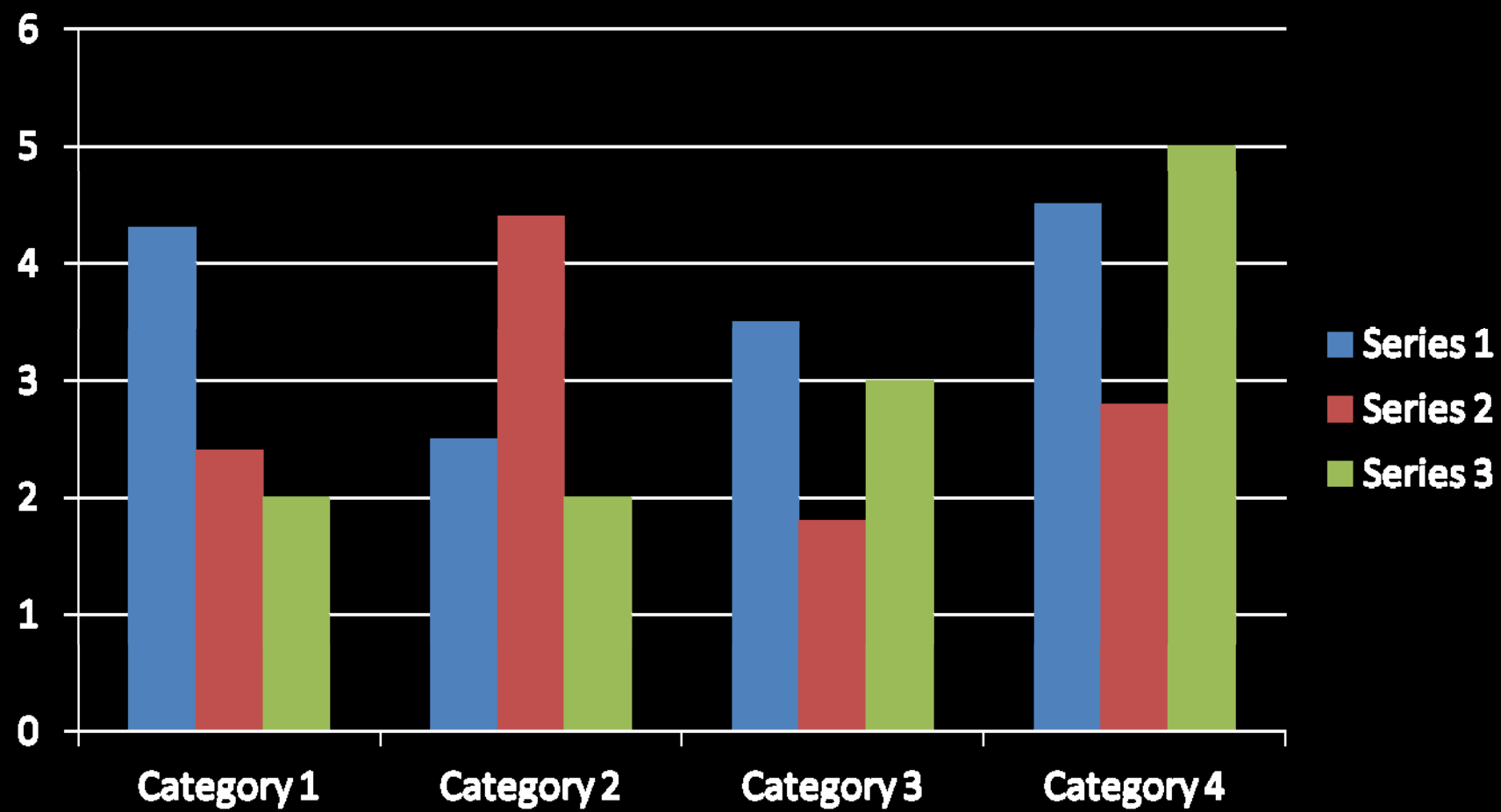Assist. Prof. Smonporn Boonyaratvej Srisongmeung

Dr. Sukit Yamwong

The Heart association of Thailand

Sanofi-Aventis

Astra Zeneca

REACH Registry Inclusion Criteria[1]

Must include:

Signed written informed consent

Patients aged ≥45 years

At least 1 of four criteria

1. **Documented cerebrovascular disease Ischemic stroke or TIA**

2. **Documented coronary disease Angina, MI, angioplasty/ stent/bypass**

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

4. **At least 3 atherothrombotic risk factors**

1. **Male aged ≥65 years or female aged ≥70 years**

2. **Current smoking >15 cigarettes/day**

3. **Type 1 or 2 diabetes**

4. **Hypercholesterolemia**

5. **Diabetic nephropathy**

6. **Hypertension**

7. **ABI <0.9 in either leg at rest**

8. **Asymptomatic carotid stenosis ≥70%**

9. **Presence of at least one carotid plaque**

1. Ohman EM et al, on behalf of the REACH Registry Investigators. *Am Heart J* 2006; *in press*.

REACH Registry Exclusion Criteria[1]

- **Anticipated difficulty in patient returning for follow-up visit**

- **Patient is currently hospitalized**

- **Patient is currently participating in a clinical trial**

1. Ohman EM et al, on behalf of the REACH Registry Investigators.
   Am Heart J 2006; *in press*.

Physician Selection: Reflection of Each Country's Management of Cardiovascular Risk[1]

	Participating physicians
How were they selected?	**Pre-defined at start of Registry** **Based on local practice population** • **General practitioners (GPs), specialists** **Mainly office-based, some hospital representation**
What is their profile?	**Representative of:** • **Local environment** • **Country geography**

1. Ohman EM et al, on behalf of the REACH Registry Investigators. *Am Heart J* 2006; *in press*.

Patient Selection: Patients Fitting Inclusion Criteria[1]

Patients

How were they selected?

Recruitment at each site

Maximum per site determined at local level (subject to central guidelines)

Within overall Registry timelines

What is their profile?

Patient inclusion criteria
- **Documented atherothrombotic disease, or with at least 3 atherothrombotic risk factors**

Real-life setting

1. Ohman EM et al, on behalf of the REACH Registry Investigators.
   Am Heart J 2006; *in press*.

A Large and Far-Reaching International Survey of Atherothrombosis*[1]

Europe: 23,542

Austria: 1,588	Lithuania: 99
Belgium: 383	The Netherlands: 324
Bulgaria: 996	Portugal: 218
Denmark: 422	Romania: 2,009
Finland: 311	Russia: 999
France: 4,592	Spain: 2,515
Germany: 5,521	Switzerland: 695
Greece: 699	Ukraine: 596
Hungary: 657	United Kingdom: 618

Asia: 10,951

China: 708
Hong Kong: 175
Indonesia: 499
Japan: 5,048
Malaysia: 525
Philippines: 1,039
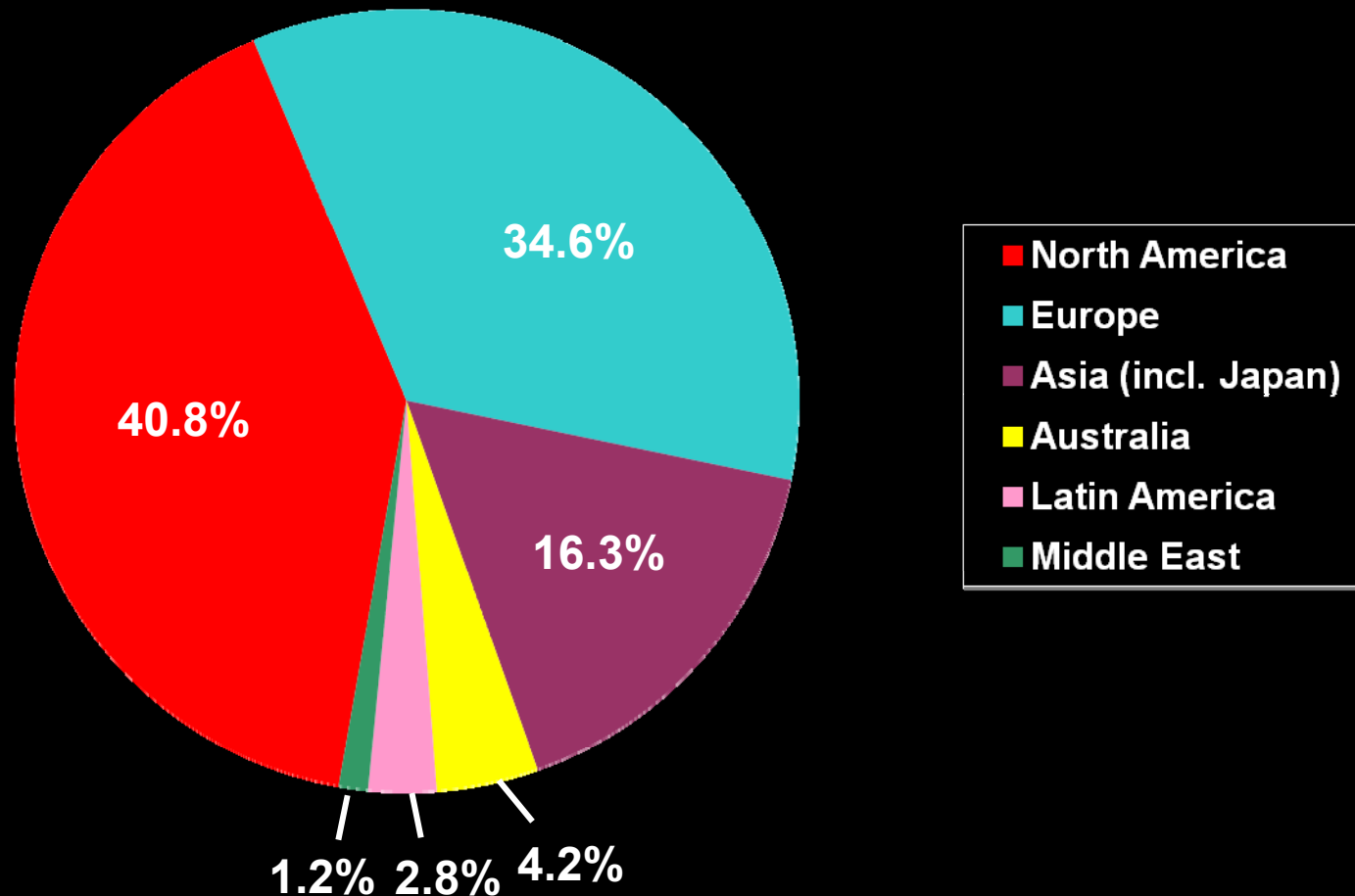Singapore: 880
South Korea: 505
Taiwan: 1,057
Thailand: 515

North America: 27,746

Canada: 1,976
USA: 25,770

Latin America: 1,931

Brazil: 441
Chile: 253
Mexico: 899

Interlatina†: 338

Middle East: 846

Israel: 379
Kingdom of Saudi Arabia: 198
Lebanon: 120
United Arab Emirates: 149

Australia: 2,872

*Data shown may differ slightly from published abstracts owing to subsequent database lock.

†Interlatina includes Panama, Costa Rica, Dominican Republic, Ecuador, Guatemala and Peru

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

Broad Geographic Representation

Geographic location of patients included in the initial analysis[1]

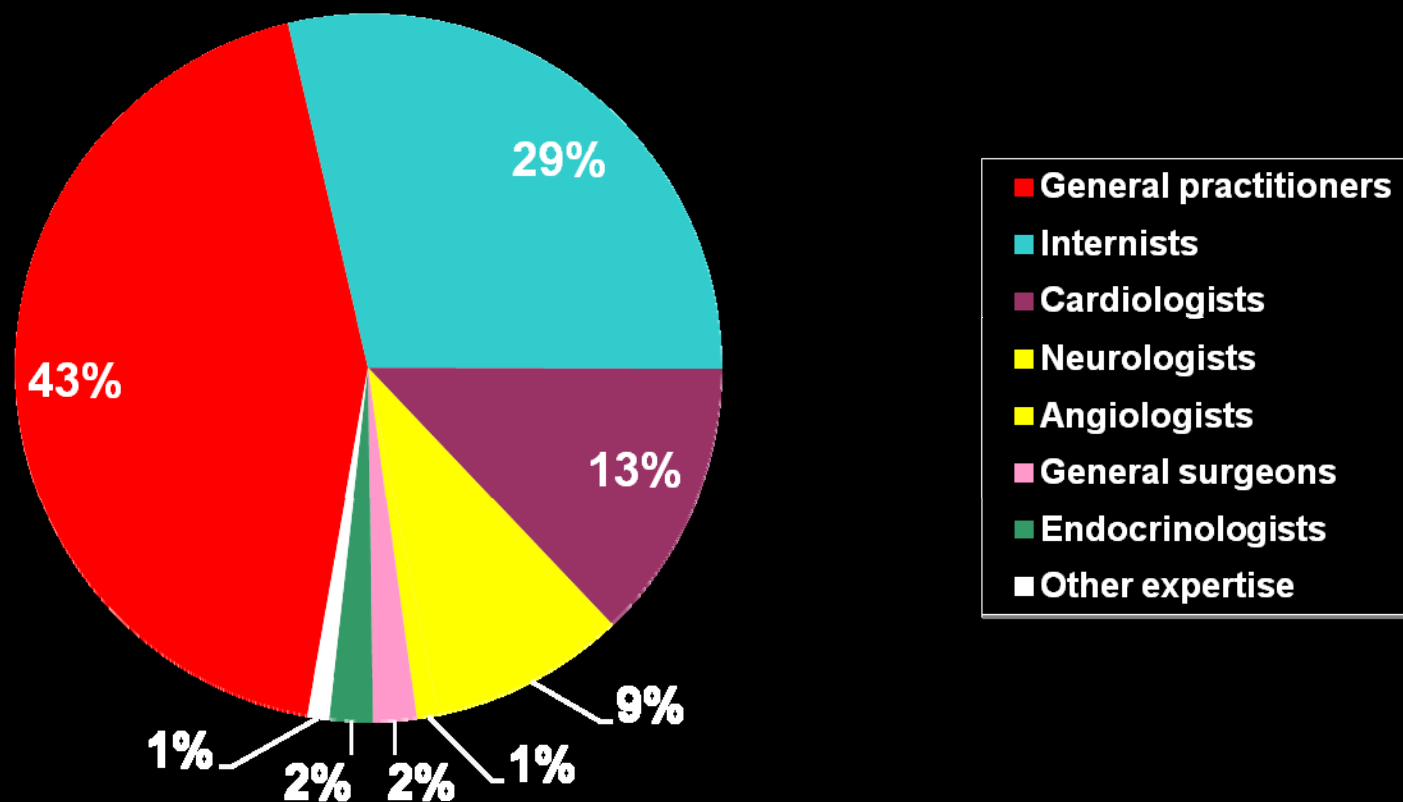|	
■	North America
■	Europe
■	Asia (incl. Japan)
■	Australia
■	Latin America
■	Middle East

34.6%

40.8%

16.3%

1.2%   2.8%   4.2%

*Data shown may differ slightly from published abstracts owing to a subsequent database lock.

1. Ohman EM et al, on behalf of the REACH Registry Investigators.
   Am Heart J 2006; *in press*.

Primary Care Practitioners (GPs and internists) Formed the Majority of REACH Registry investigators

REACH Registry Investigators by specialty (% of total)[1]

Legend:
- General practitioners
- Internists
- Cardiologists
- Neurologists
- Angiologists
- General surgeons
- Endocrinologists
- Other expertise

Pie chart values: 43%, 29%, 13%, 9%, 1%, 2%, 2%, 1%

*Data shown may differ slightly from published abstracts owing to a subsequent database lock.

1. Ohman EM et al, on behalf of the REACH Registry Investigators.
   Am Heart J 2006; *in press*.

High Prevalence of Polyvascular Disease
(Disease in More Than One Arterial Bed)

$\sim$ 1/4 of Patients with CAD Have Polyvascular Disease[1]

~ 1/4 of the 40,258 patients with CAD also have atherothrombotic disease in other arterial territories

(%s are of total population)[1]

RISK FACTORS ONLY

Coronary Artery Dis

44.6%

8.4%

1.6%

Cerebro-vascular

4.7%

Periph Art Disease

Patients with CAD = 59.3% of the REACH Registry population
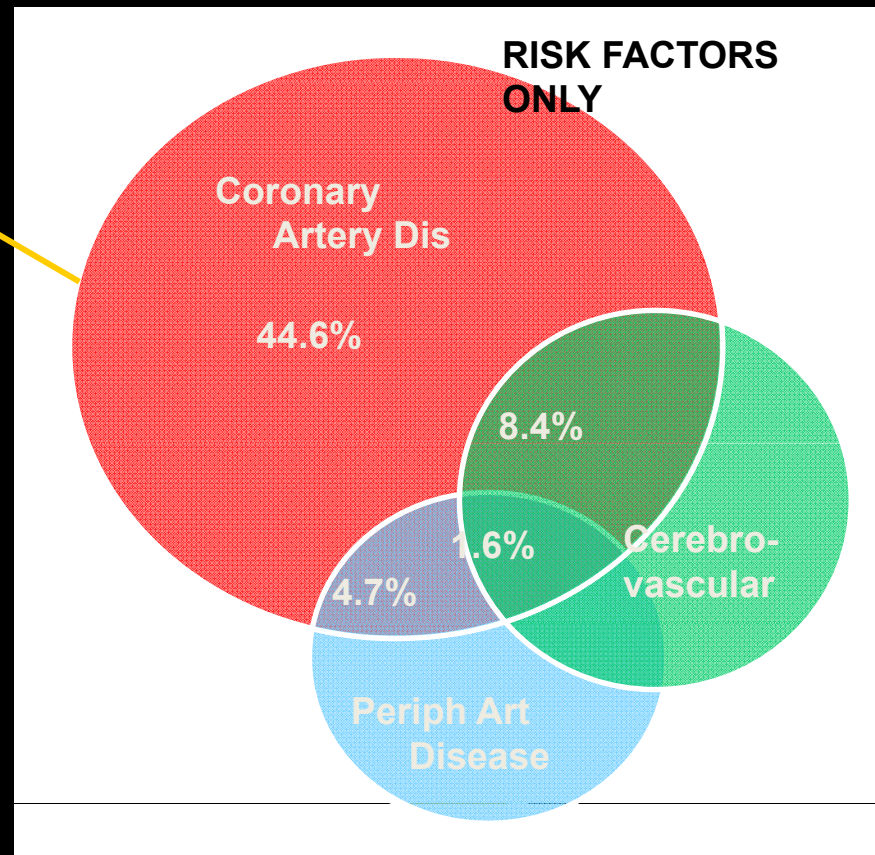
1. Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006; 295(2): 180-189.

~ 2/5 of Patients with Cerebrovascular Disease Have Polyvascular Disease[1]

~ 2/5 of the 18,843 patients with Cerebrovascular Disease also have atherothrombotic disease in other arterial territories

(%s are of total population)[1]

RISK FACTORS ONLY

Coronary Artery Dis

Cerebro-vascular

Periph Art Disease

8.4%

1.6%

16.6%

1.2%

Patients with Cerebrovasc Dis = 27.8% of the REACH Registry population
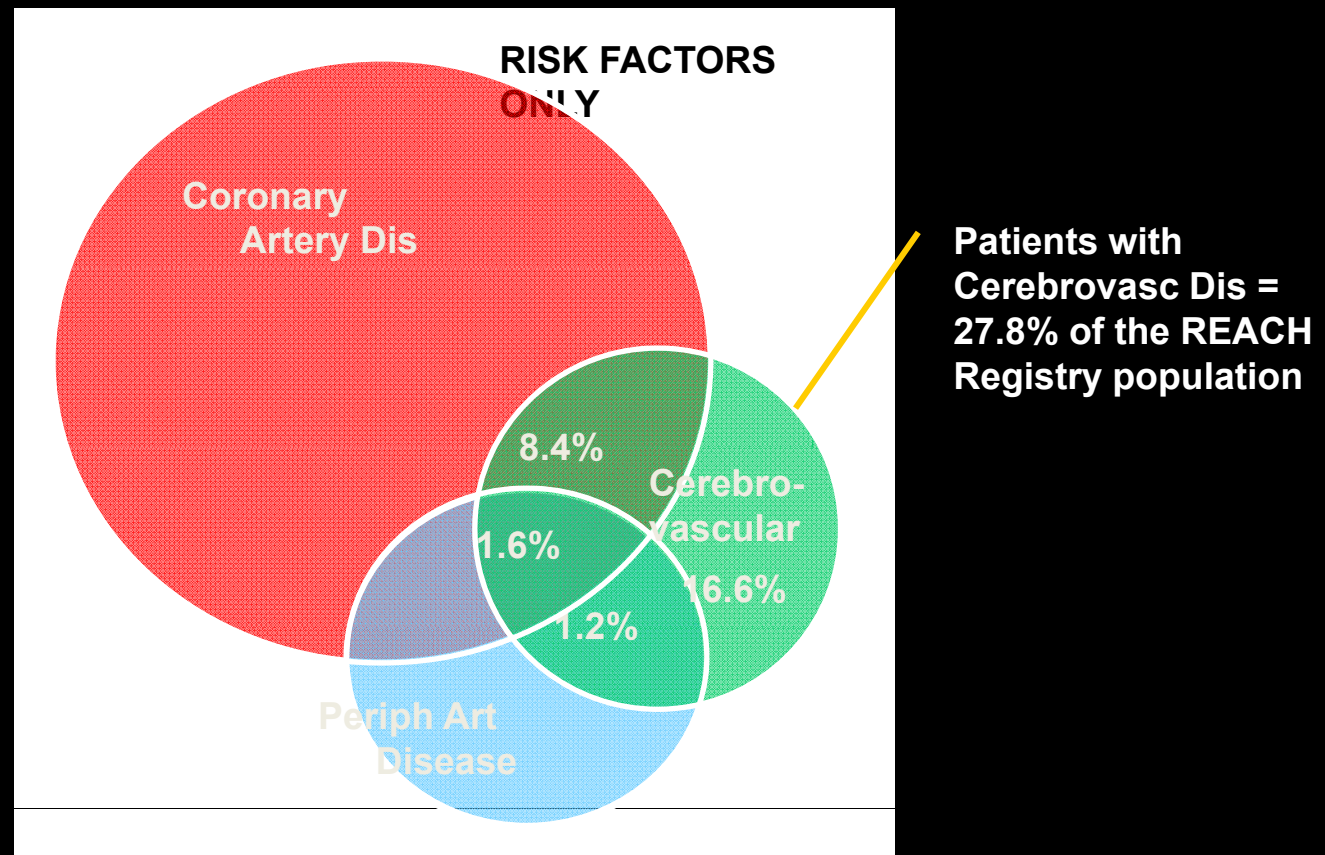
1. Bhatt DL et al, on behalf of the REACH Registry Investigators. *JAMA* 2006; 295(2): 180-189.

~ 3/5 of Patients with Symptomatic PAD Have Polyvascular Disease[1]

~ 3/5 of the 8,273 patients with PAD also have atherothrombotic disease in other arterial territories

(%s are of total population)[1]

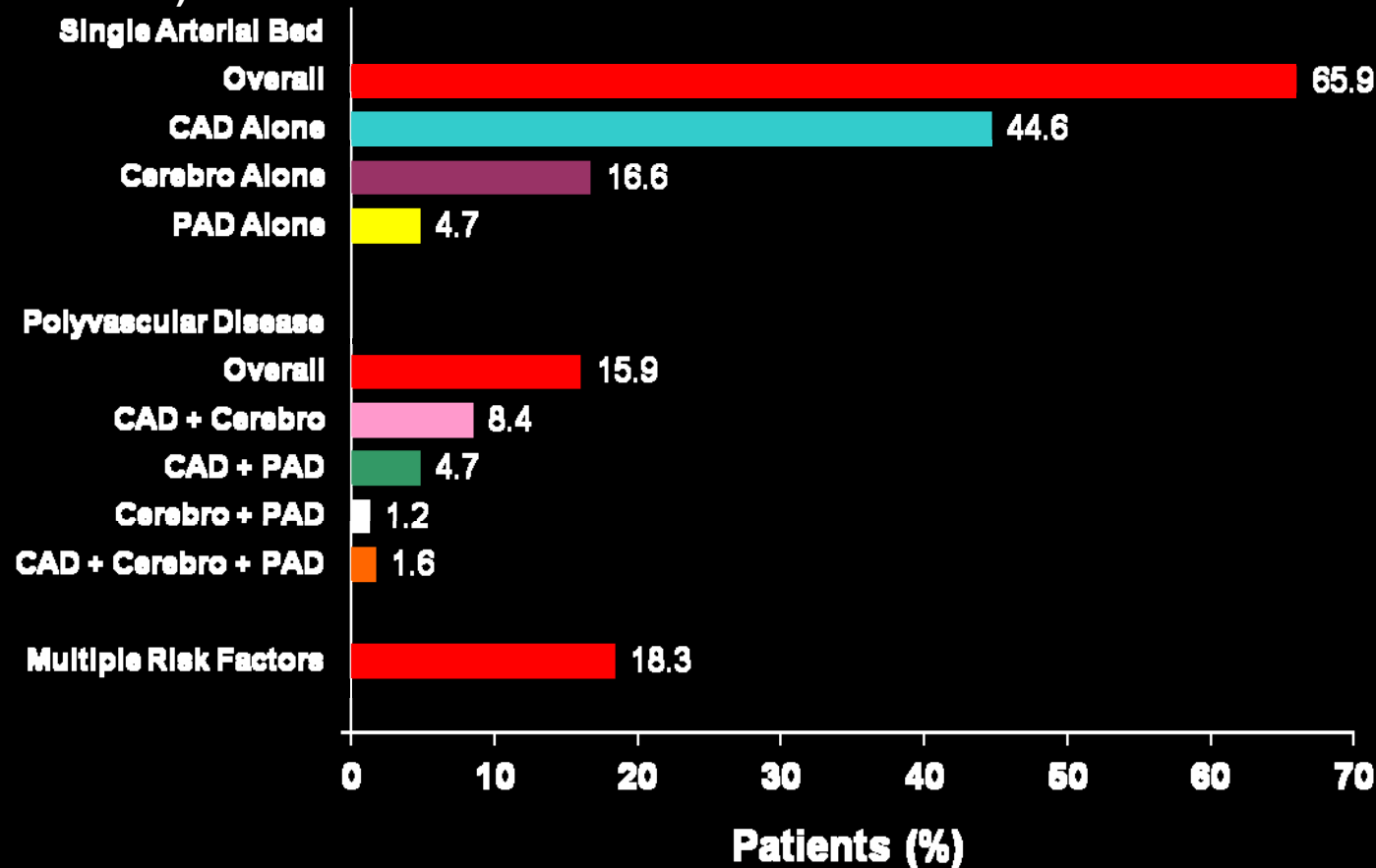Patients with PAD = 12.2% of the total REACH Registry population

RISK FACTORS ONLY

Coronary Artery Dis

Cerebro-vascular

4.6%

4.7%

1.2%

Periph Art Disease 4.7%
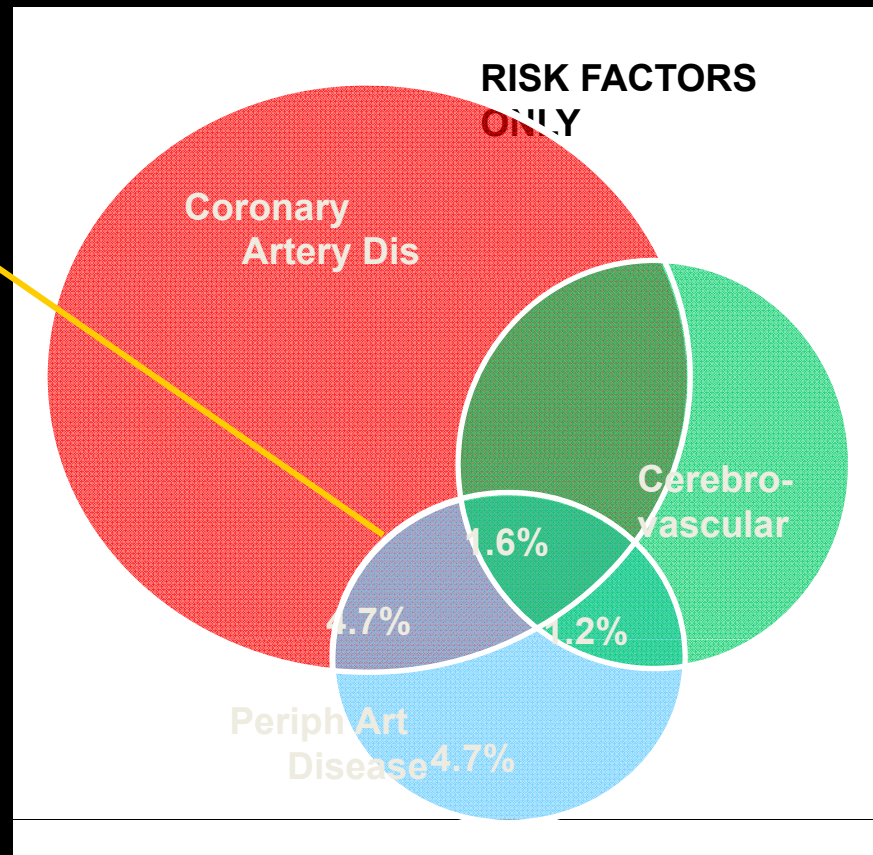
1. Bhatt DL et al, on behalf of the REACH Registry Investigators.
   JAMA 2006; 295(2): 180-189.

A Large Minority had Polyvascular Disease in the REACH Registry*[1]

Prevalence of disease in arterial beds

(% of total)[1]

*Data shown may differ slightly from published abstracts owing to a subsequent database lock.
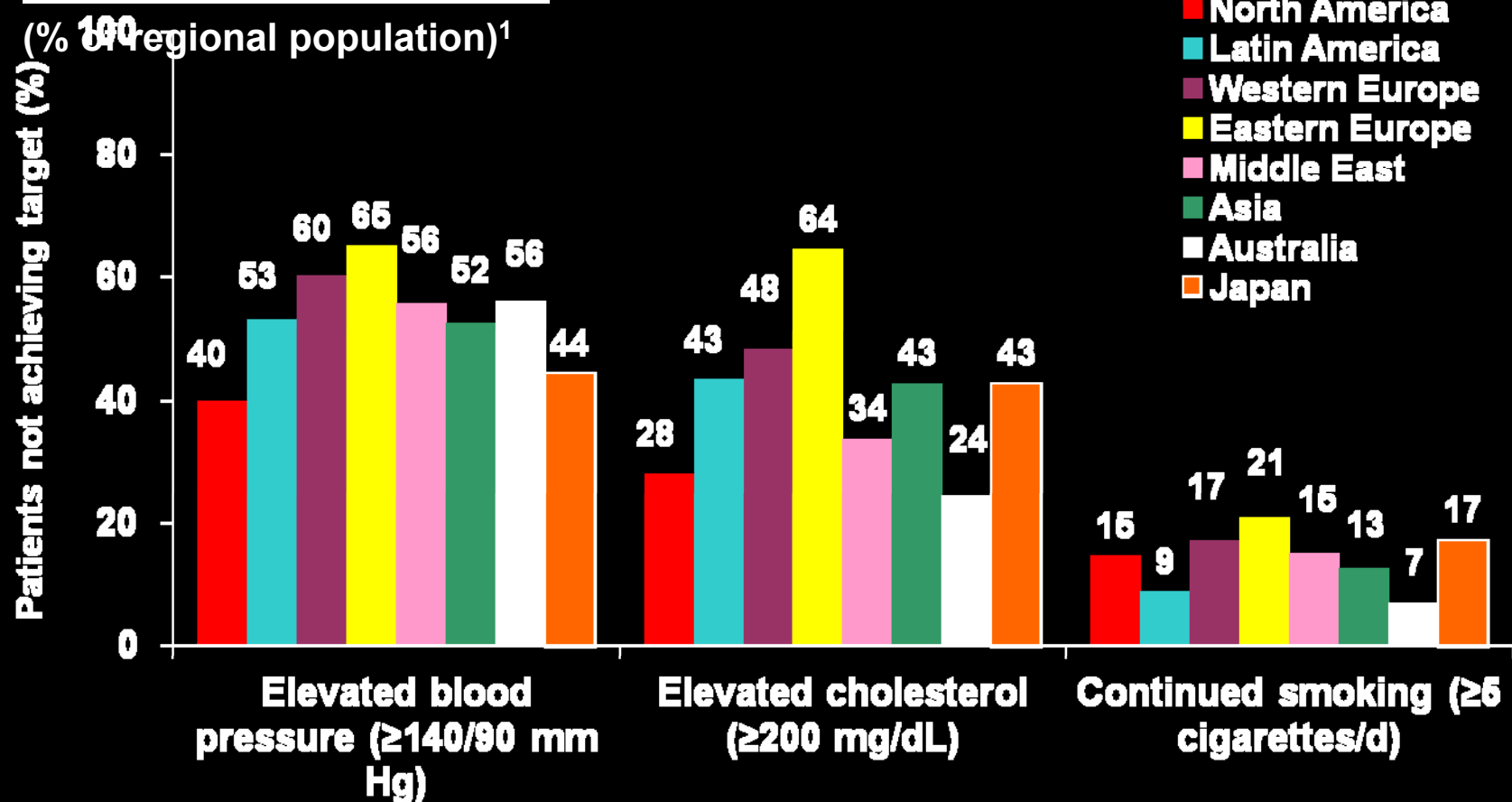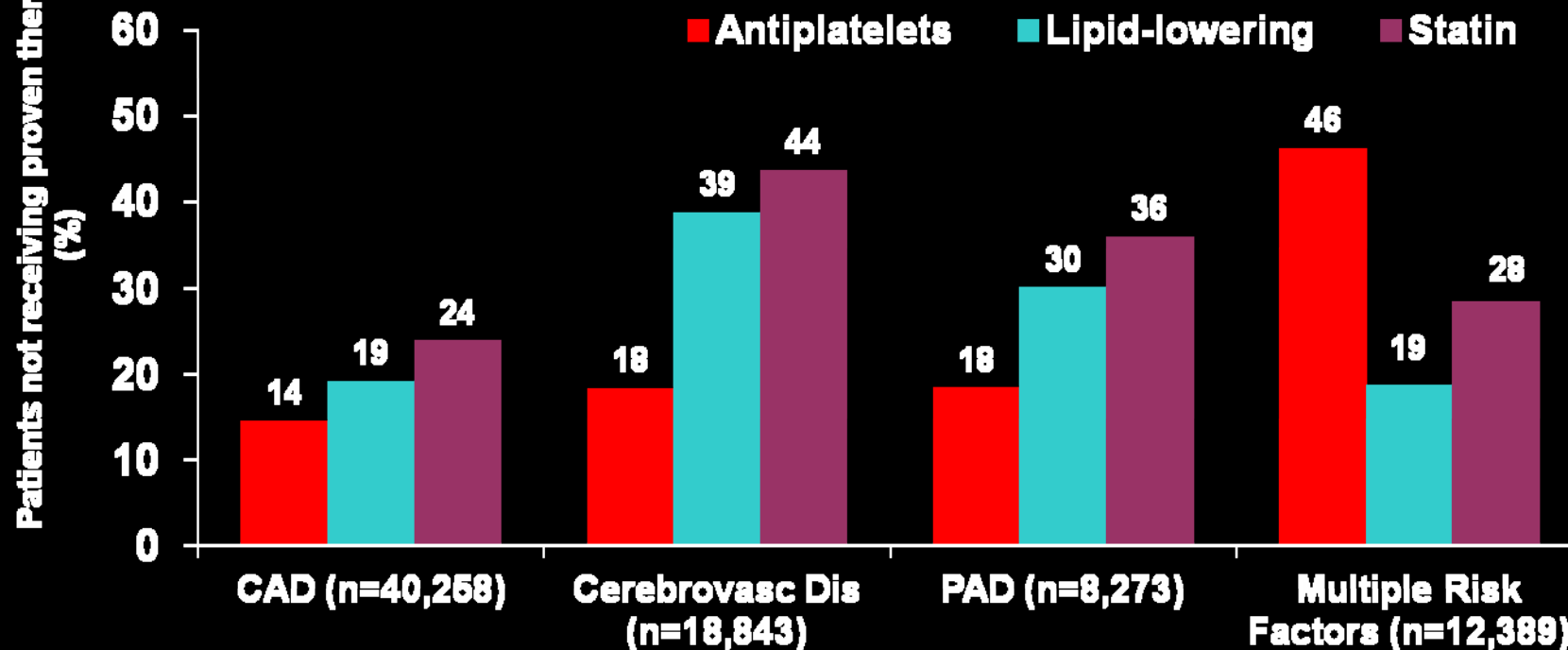
1. Bhatt DL et al, on behalf of the REACH Registry Investigators.
   JAMA 2006; 295(2): 180-189.

Undertreatment of Patients with Atherothrombosis Worldwide

Undertreatment of Risk Factors in Patients Worldwide*[1]

Patients not achieving target (% of regional population)[1]

Legend:
- North America
- Latin America
- Western Europe
- Eastern Europe
- Middle East
- Asia
- Australia
- Japan

Y-axis: Patients not achieving target (%)

Elevated blood pressure (≥140/90 mm Hg): 40, 53, 60, 65, 56, 52, 56, 44

Elevated cholesterol (≥200 mg/dL): 28, 43, 48, 64, 34, 43, 24, 43

Continued smoking (≥5 cigarettes/d): 15, 9, 17, 21, 15, 13, 7, 17
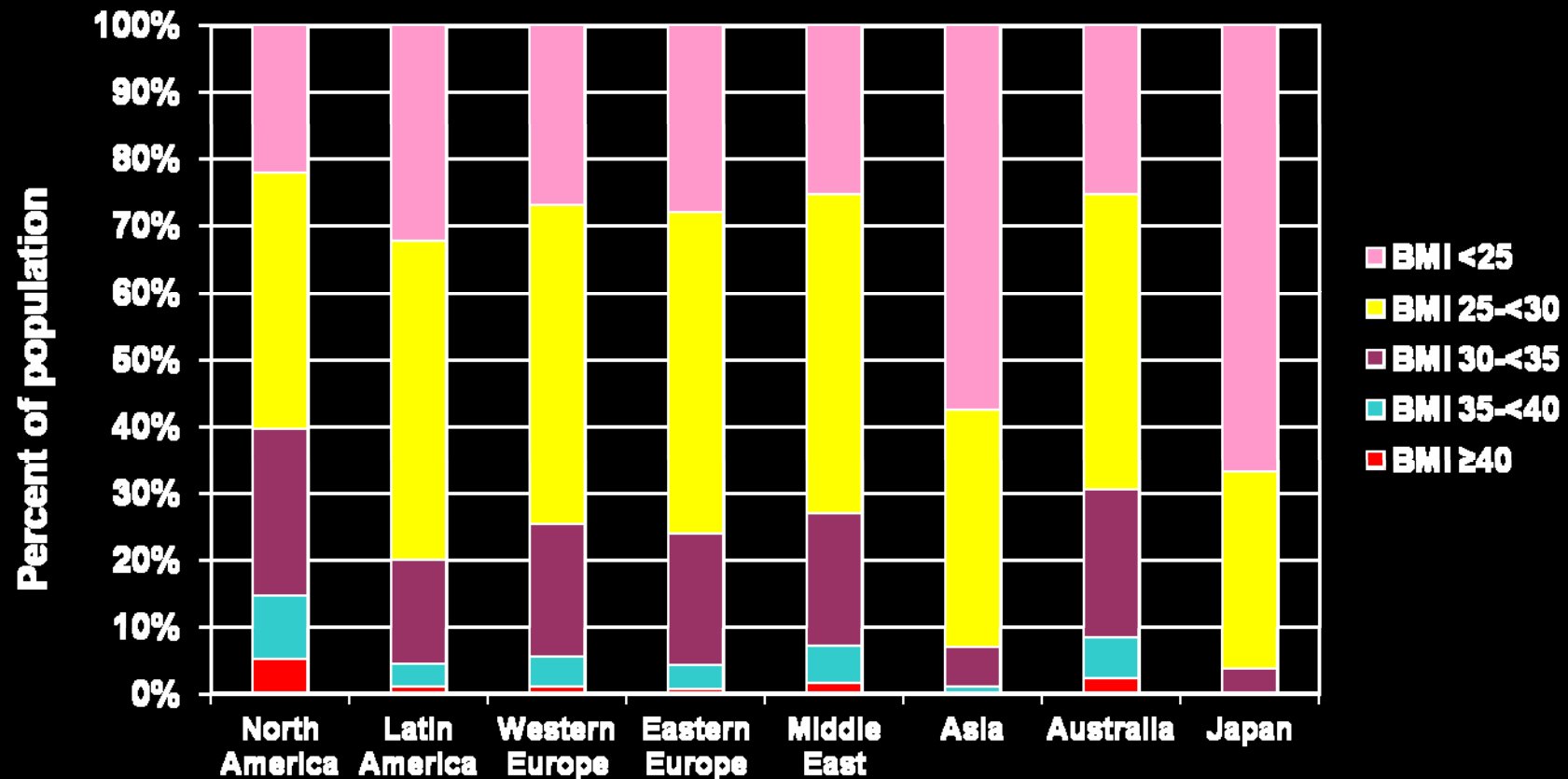
*Data shown may differ slightly from published abstracts owing to a subsequent database lock.

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

Established Therapies are Consistently Underused in All Patient Types*[1]

Patients not receiving therapy

(% of subpopulation)[1]

Data shown may differ slightly from published abstracts owing to a subsequent database lock.

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

High Prevalence of Overweight and Obesity in Most Regions[*][1]

Variation of overweight and obesity in the symptomatic population**
(% of regional population)[1]

Legend:
- BMI <25
- BMI 25–<30
- BMI 30–<35
- BMI 35–<40
- BMI ≥40

Regions: North America, Latin America, Western Europe, Eastern Europe, Middle East, Asia, Australia, Japan

Y-axis: Percent of population

*Data shown may differ slightly from published abstracts owing to a subsequent database lock;
**Symptomatic refers to patients with documented CAD, Cerebrovasc Dis and/or PAD

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

Overweight and Obesity Highly Prevalent in Multiple Risk Factor Patients in Most Regions*[1]

Variation of Overweight and Obesity in the

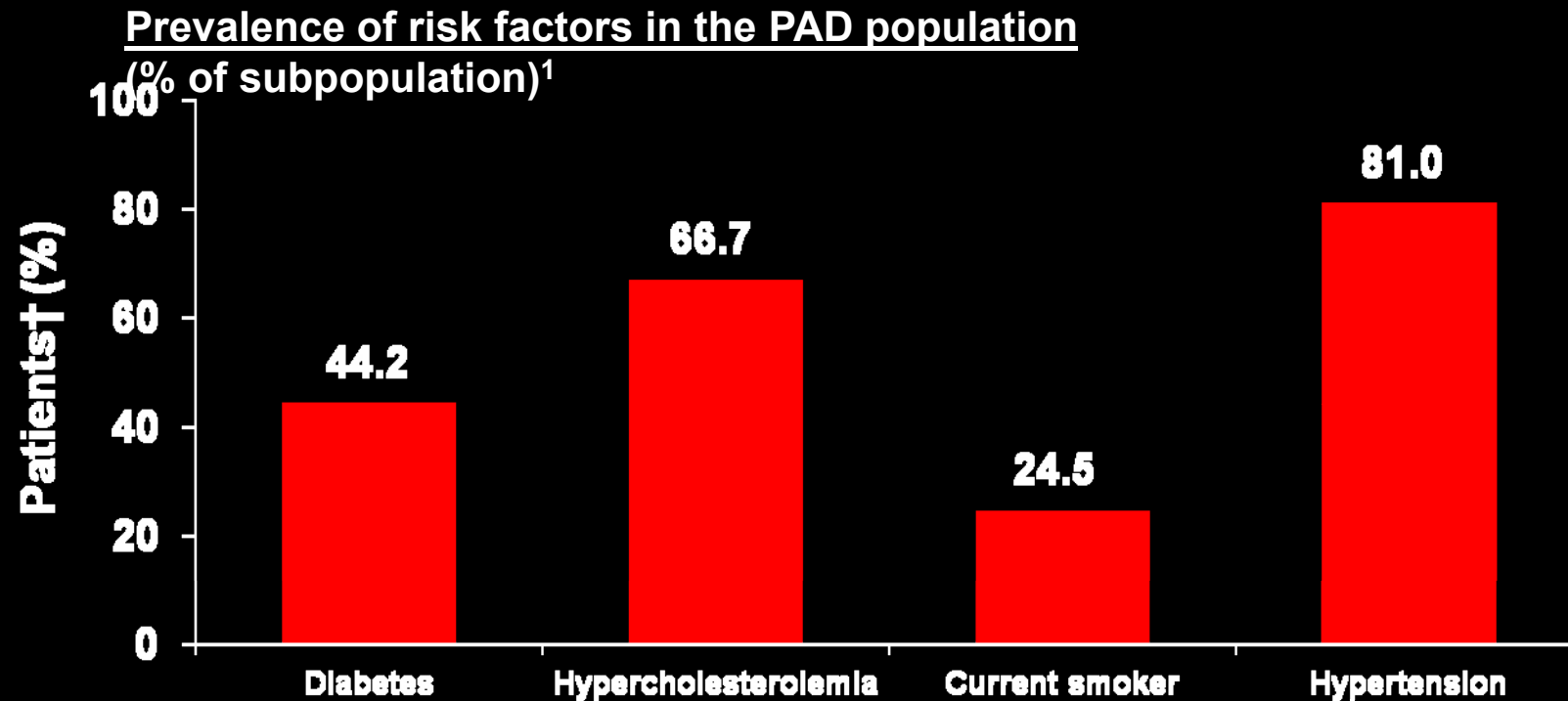**Multiple Risk Factor REACH Registry Population**

(% of regional population)[1]
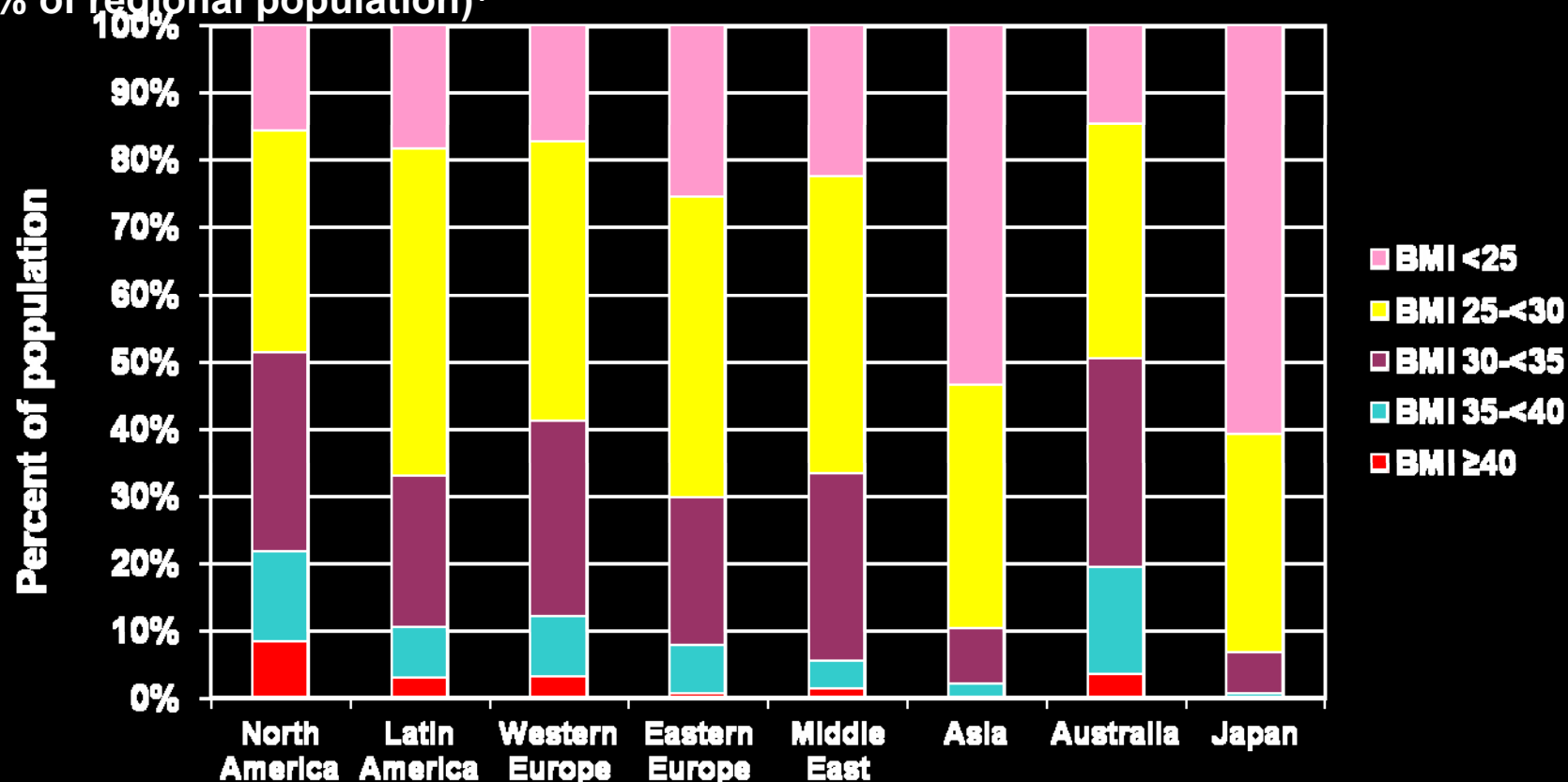
Data shown may differ slightly from published abstracts owing to a subsequent database lock.

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

High Prevalence of Concomitant Risk Factors in Patients with Symptomatic PAD*[1]

Prevalence of risk factors in the PAD population (% of subpopulation)[1]

[†]Of the 8,273 patients with symptomatic PAD, the mean age was 69.2 years and 70.7% were male

*Data shown may differ slightly from published abstracts owing to a subsequent database lock.

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

PAD Patients are Less Likely than Other Patients to Use Established Therapies*[1]

Patients receiving established therapy (% of patients)[1]
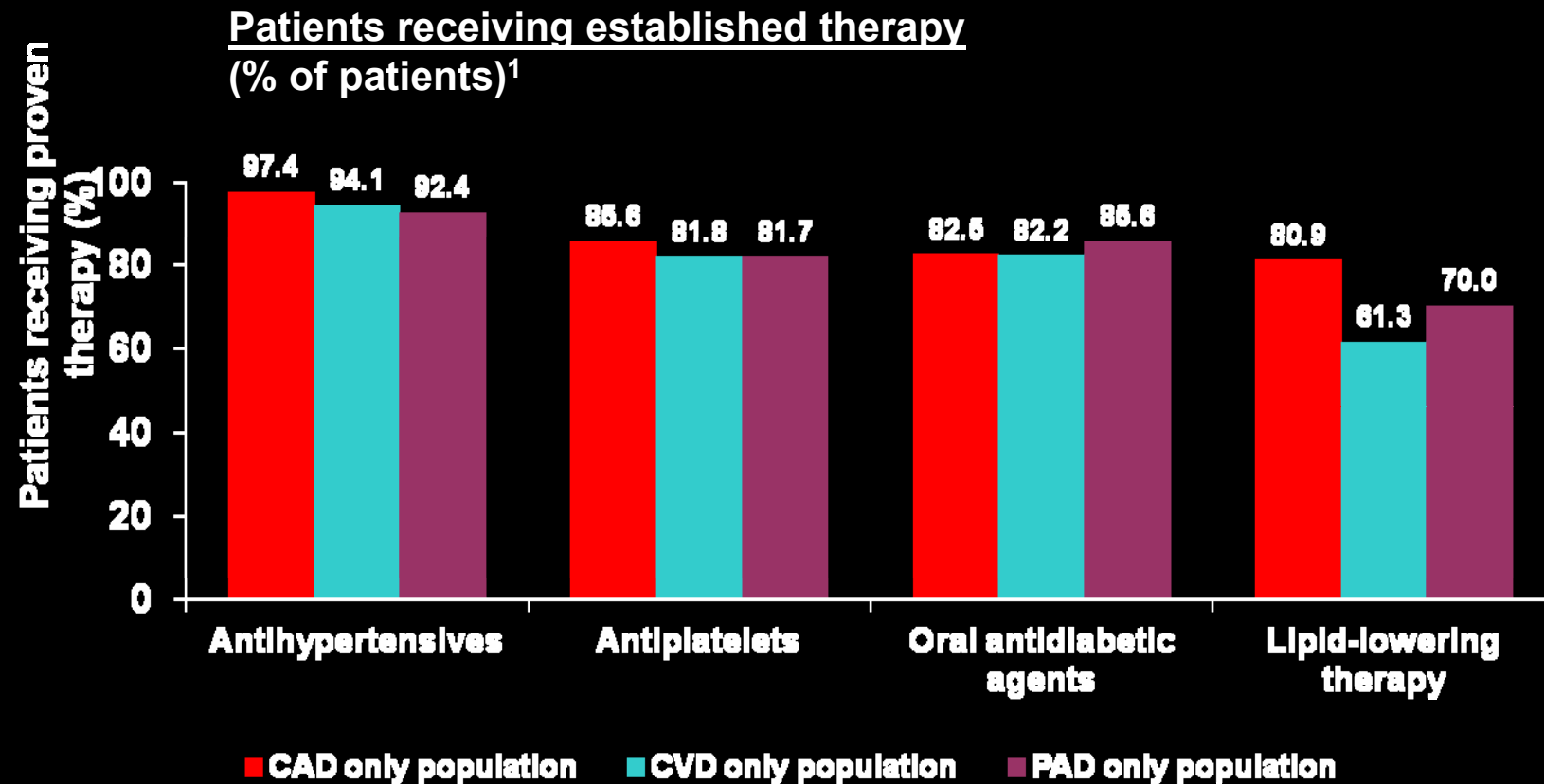
For antihypertensives, % is of pts diagnosed hypertension or elevated blood pressure at initial examination;
For oral antidiabetics, % is of pts with history of diabetes or elevated blood glucose at initial examination

*Data shown may differ slightly from published abstracts owing to a subsequent database lock.

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

Risk factors are consistently found across all disease sub-populations*[1]

Risk Factor Prevalence, By Sub-Population
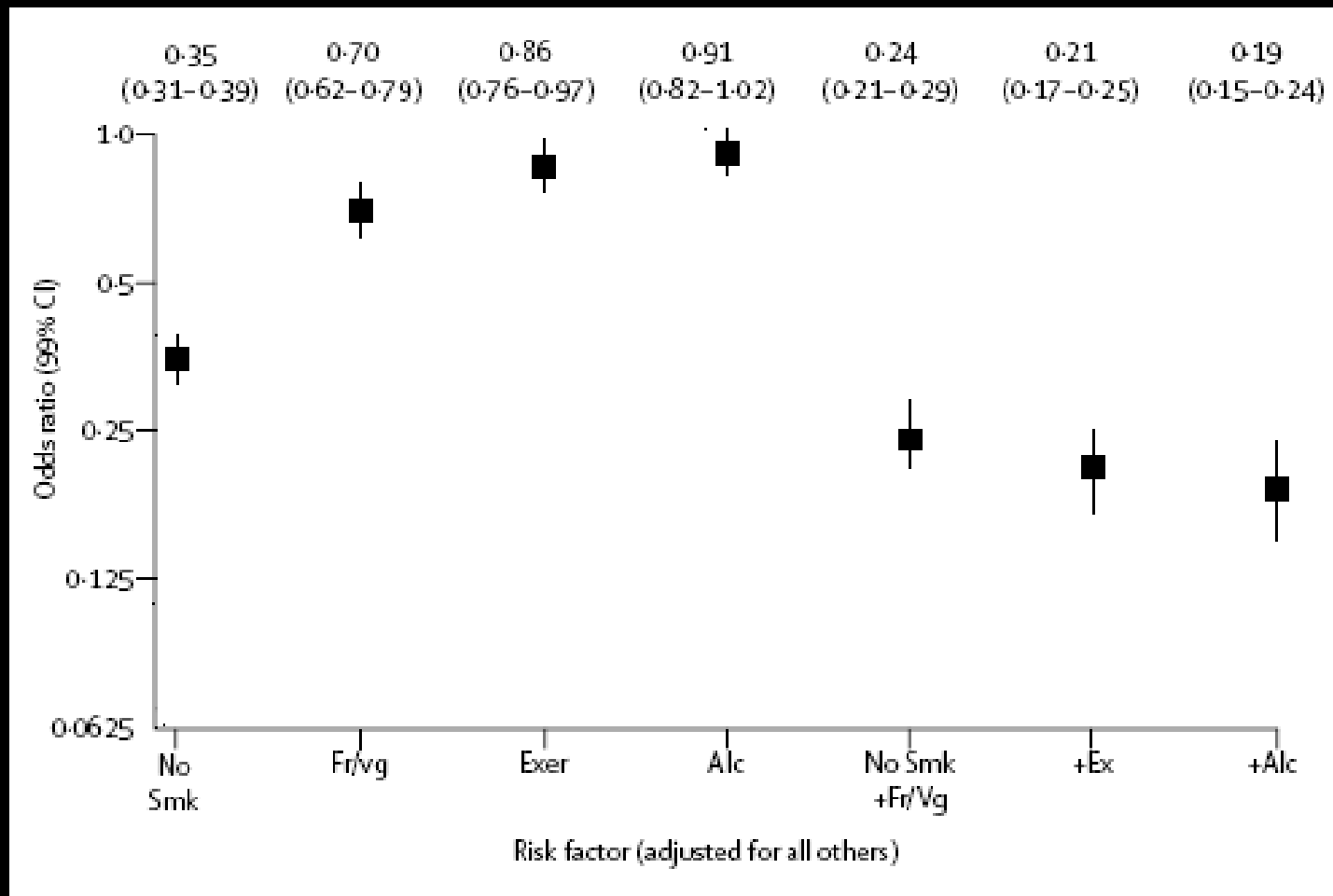**(% of MRF population)[1]**
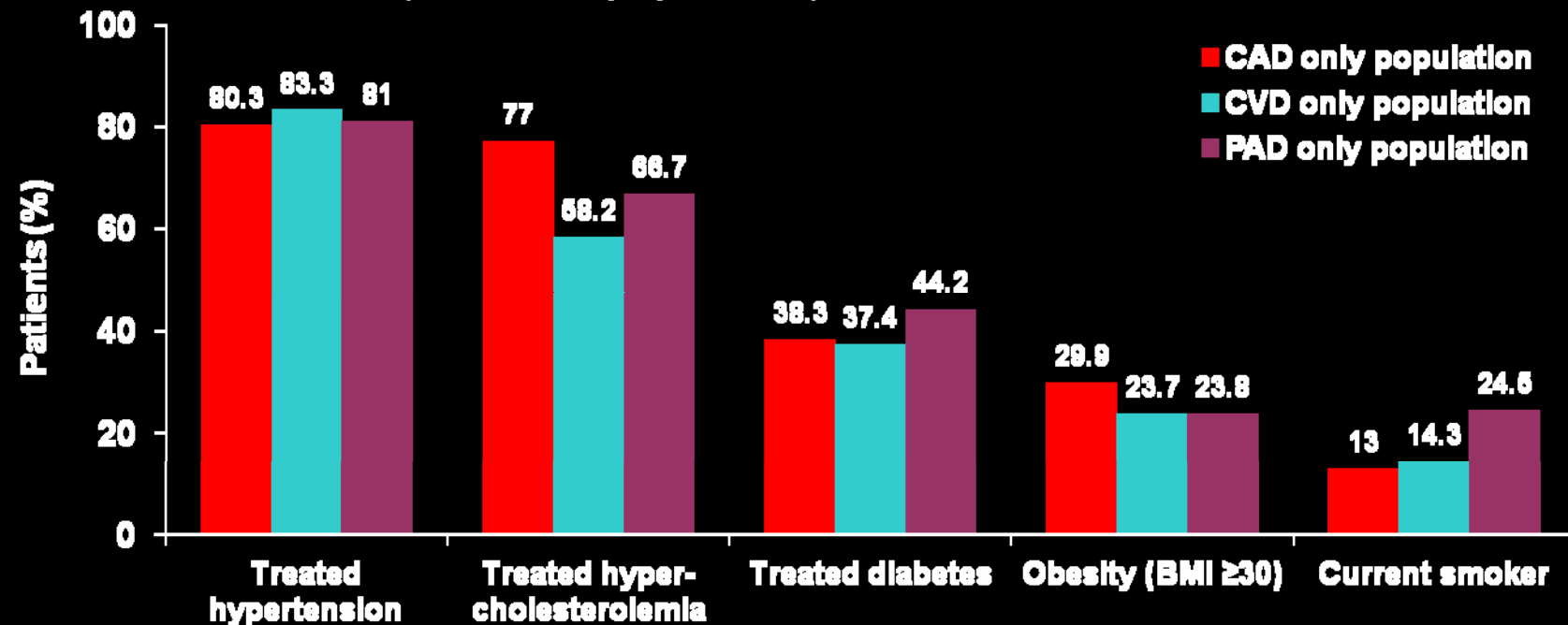
1. Bhatt DL et al, on behalf of the REACH Registry Investigators.
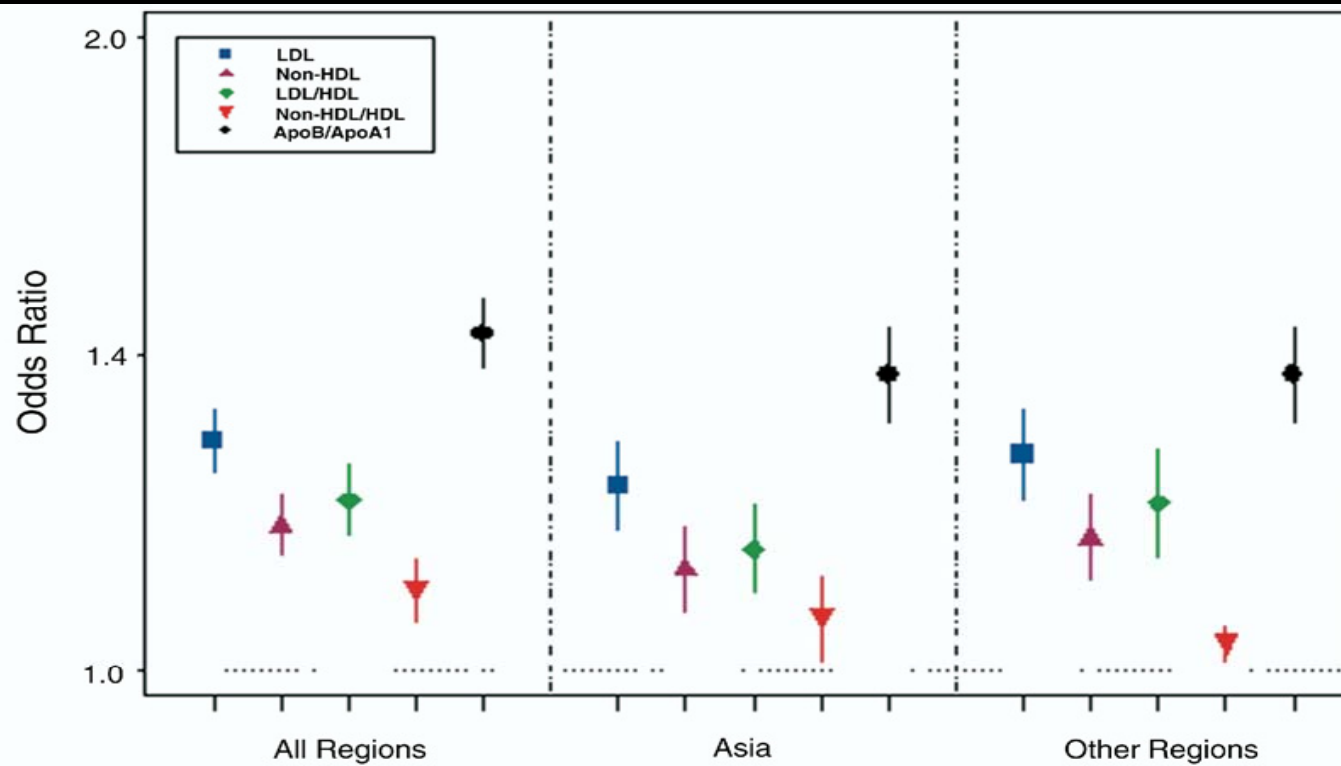   *JAMA* 2006; 295(2): 180-189.

Medications

Risk of acute myocardial infarction associated with exposure to multiple risk factors
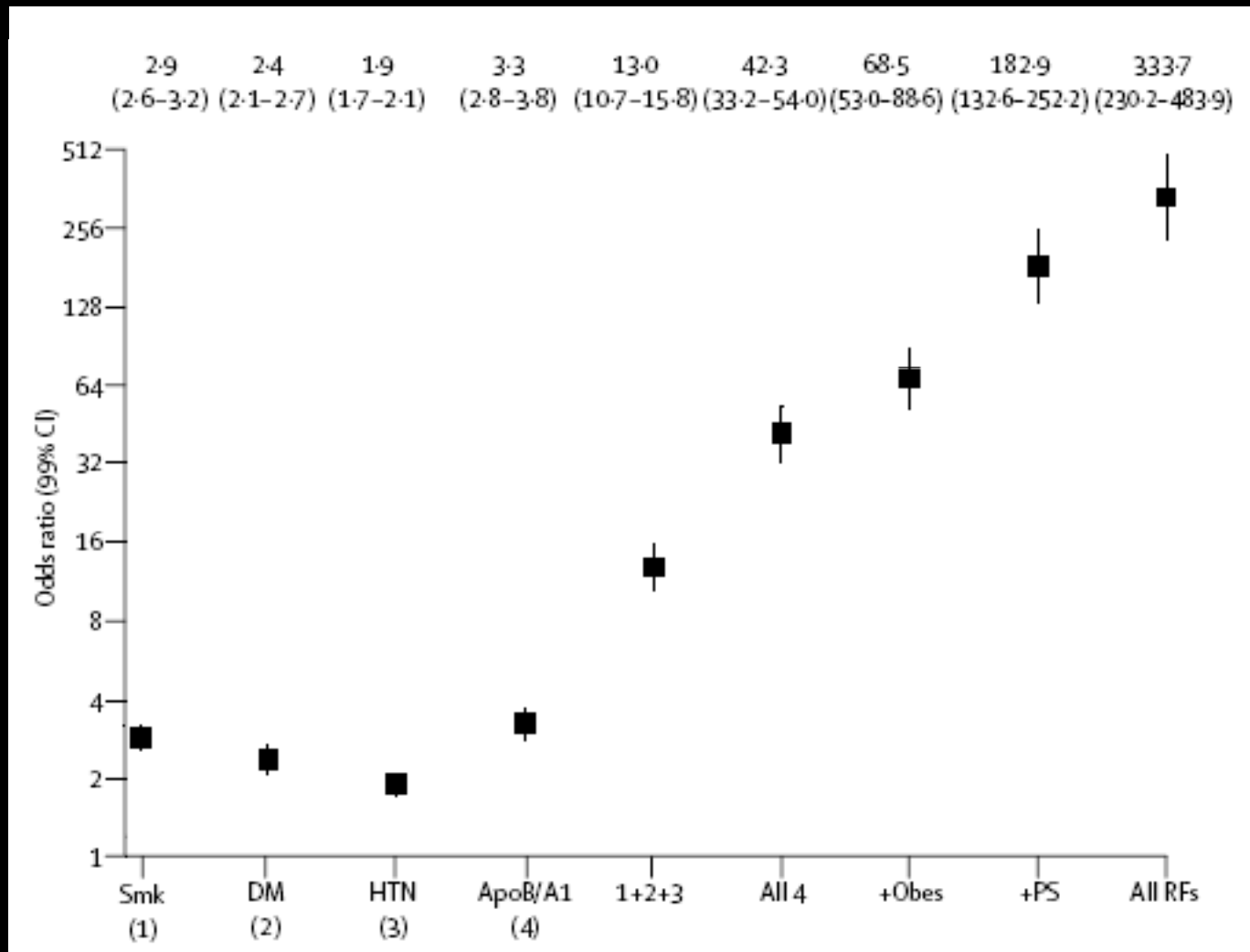
Reduced risk of acute myocardial infarction associated with various risk factors
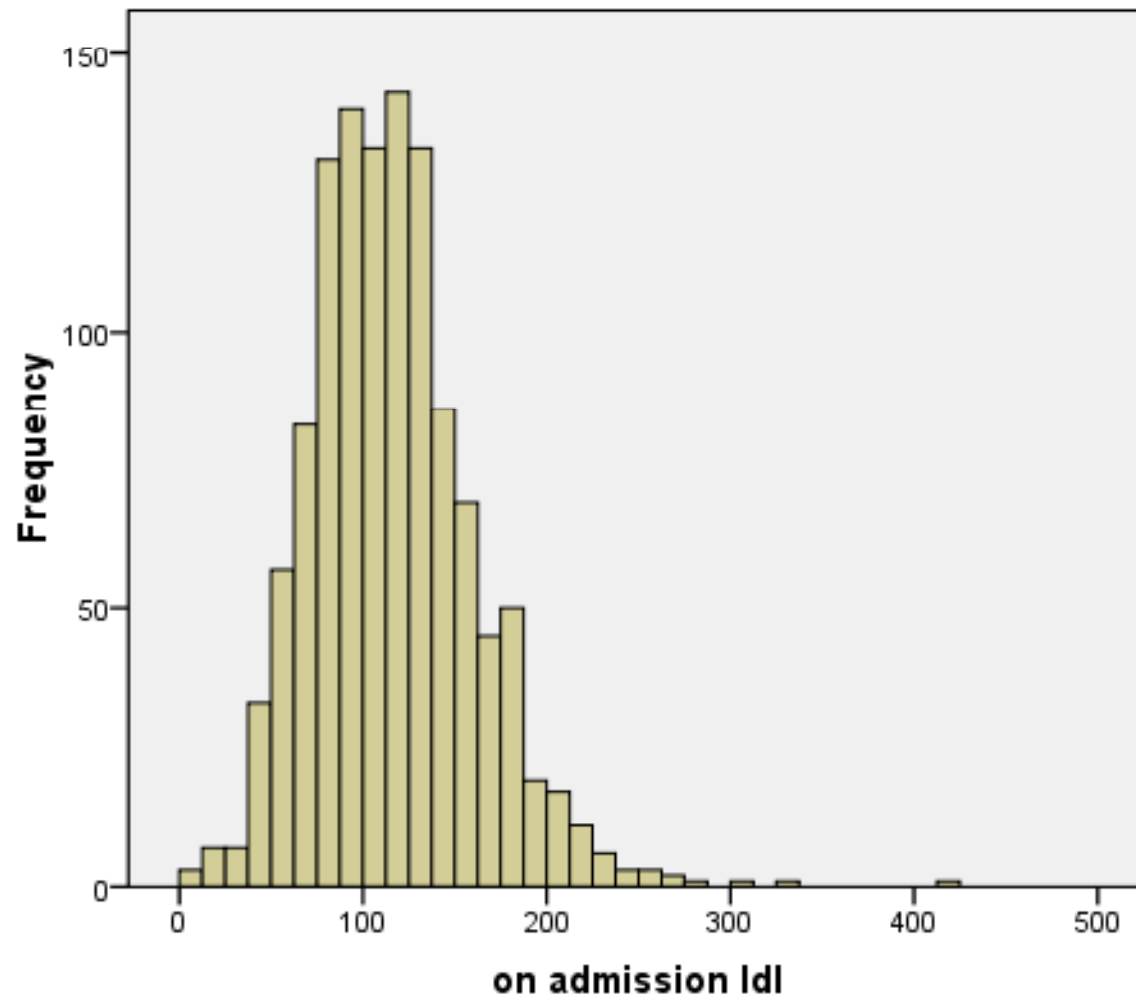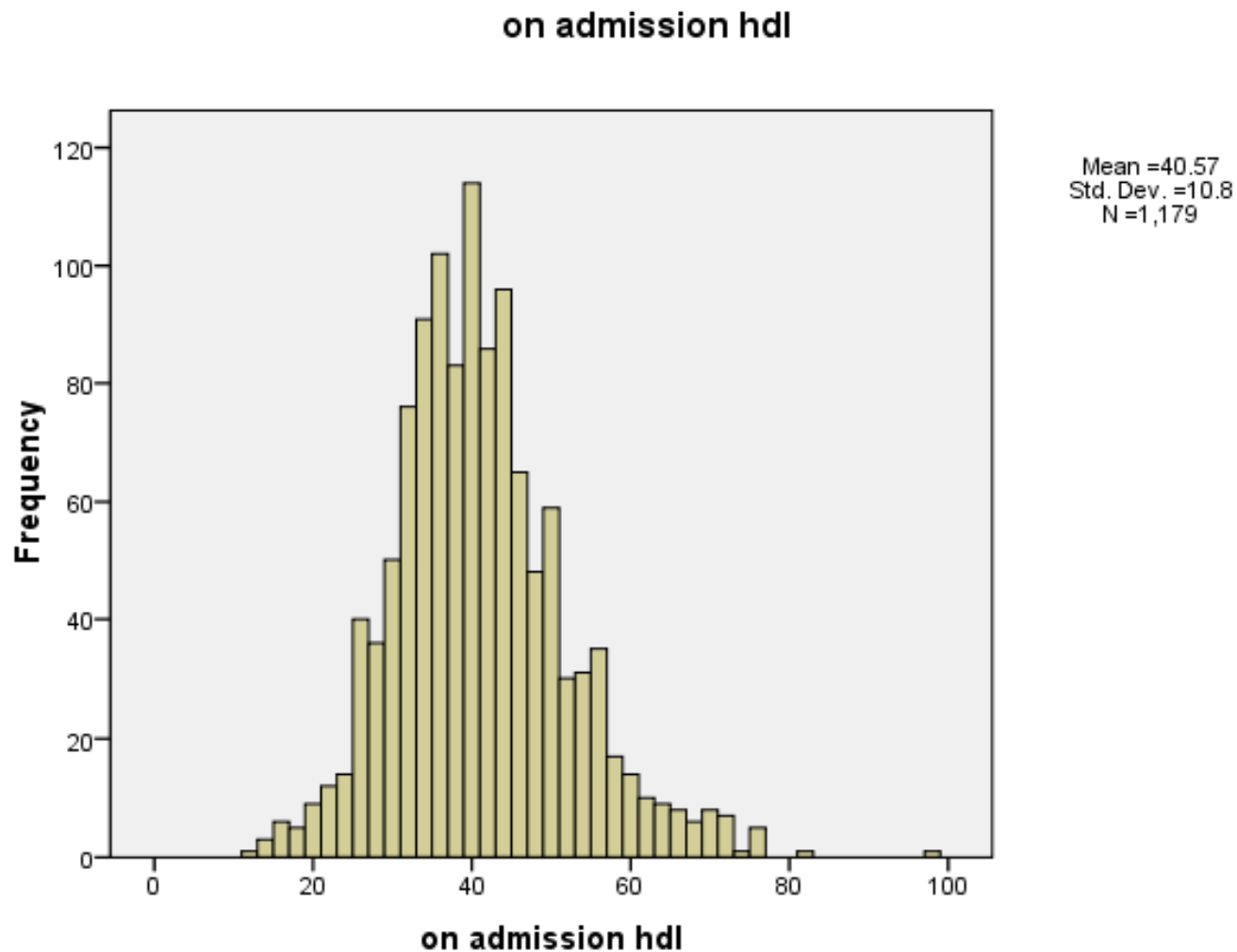
Lipid and risk of MI

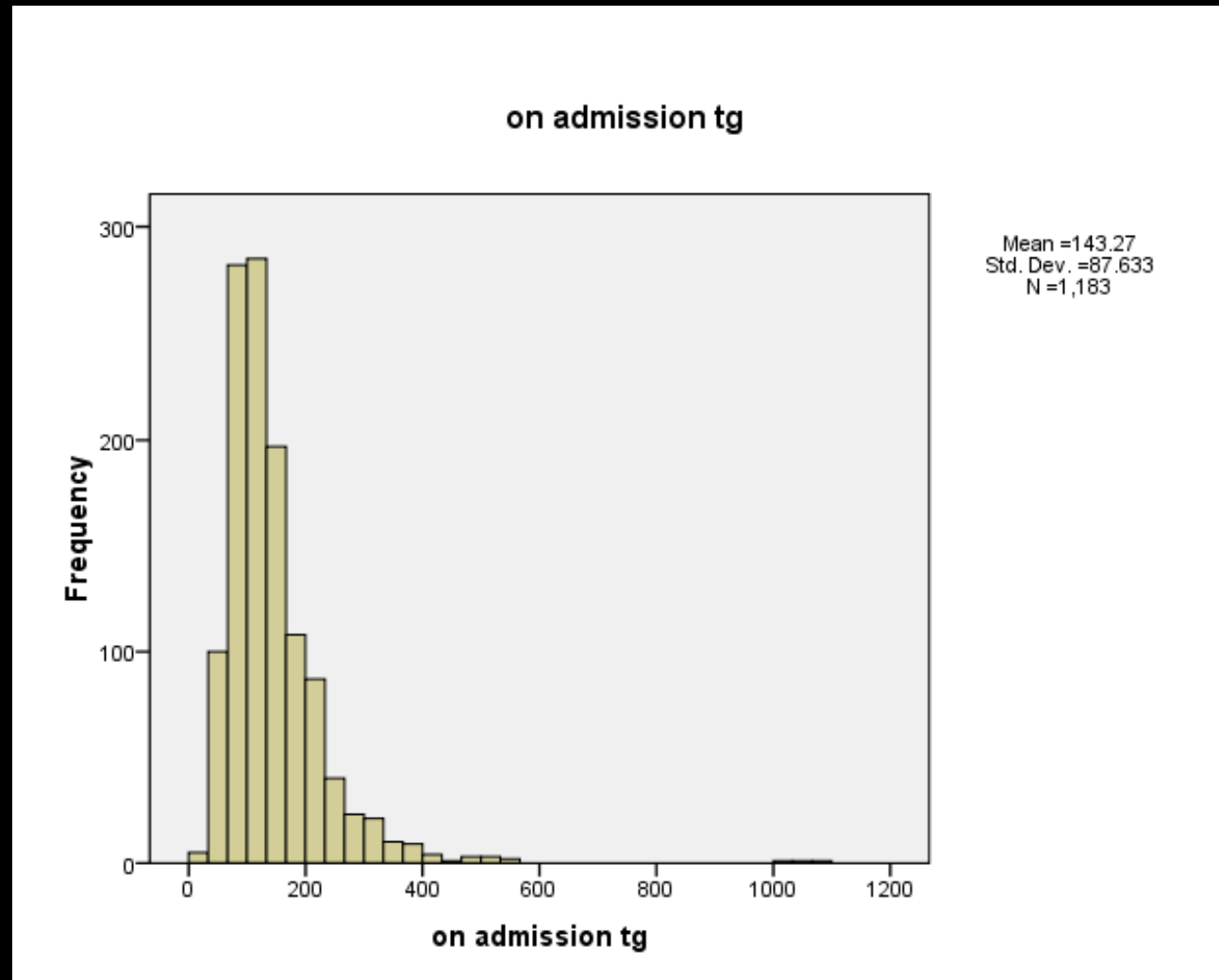|	All Regions OR* (95% CI)	Asia OR* (95% CI)	Other Regions OR* (95% CI)
LDL	1.29 (1.24-1.33)	1.22 (1.17-1.28)	1.27 (1.21-1.33)
Non-HDL	1.17 (1.14-1.21)	1.12 (1.07-1.17)	1.16 (1.11-1.21)
LDL/HDL	1.21 (1.16-1.25)	1.14 (1.09-1.20)	1.20 (1.13-1.27)
Non-HDL/HDL	1.09 (1.06-1.13)	1.06 (1.01-1.11)	1.03 (1.01-1.05)
ApoB/ApoA1	1.45 (1.39-1.50)	1.38 (1.31-1.46)	1.38 (1.31-1.46)

LDL-C in Chiang-Mai ACS

HDL-C in Chiang Mai-ACS

Triglyceride in Chiang Mai-ACS

on admission tg

มีการติดตามผู้ป่วยเป็นระยะ ดังนี้

V1 – ครั้งที่ 1 เมื่ออาสาสมัครเข้าร่วมโครงการ

V2 – ครั้งที่ 2 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 6 เดือน

V3 – ครั้งที่ 3 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 12 เดือน

V4 – ครั้งที่ 4 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 24 เดือน

V5 – ครั้งที่ 5 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 36 เดือน

V6 – ครั้งที่ 6 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 48 เดือน

V7 – ครั้งที่ 7 หลังจากอาสาสมัครเข้าร่วมโครงการเป็นเวลา 60 เดือน

Sub-study

- Population: 2000 patients from main study

- Participating hospitals: hospitals with facility for specimen collection

Current status

- 1st investigator meeting: 19 Nov. 2010

- EC/IRB approval submission

What will we get from the CORE-Thailand

With long term (at least 5 years of clinical follow-up, the CORE-Thailand will

- provide 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

- Cost-effectiveness , pharmacoeconomic

Proposed research questions

- Baseline characteristics of high atherosclerotic risk patients in Thailand

- Factors determining new cardiovascular events in the high risk patients

- Factors determine the guideline containment of risk factor control

- Risk factors control and cardiovascular events reduction

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 renal insufficiency and CV events

- The novel markers of renal injury and CV events

HDL-C in Chiang Mai-ACS

HDL-C categories	Proportion (%)
< 40mg/dl	50.1
41-50mg/dl	31.8
>51mg/dl	18.1

Atherothrombosis – a Generalized and Progressive Disease Process

Thrombosis

UA
MI } **ACS**

Ischemic stroke/TIA

Vascular death
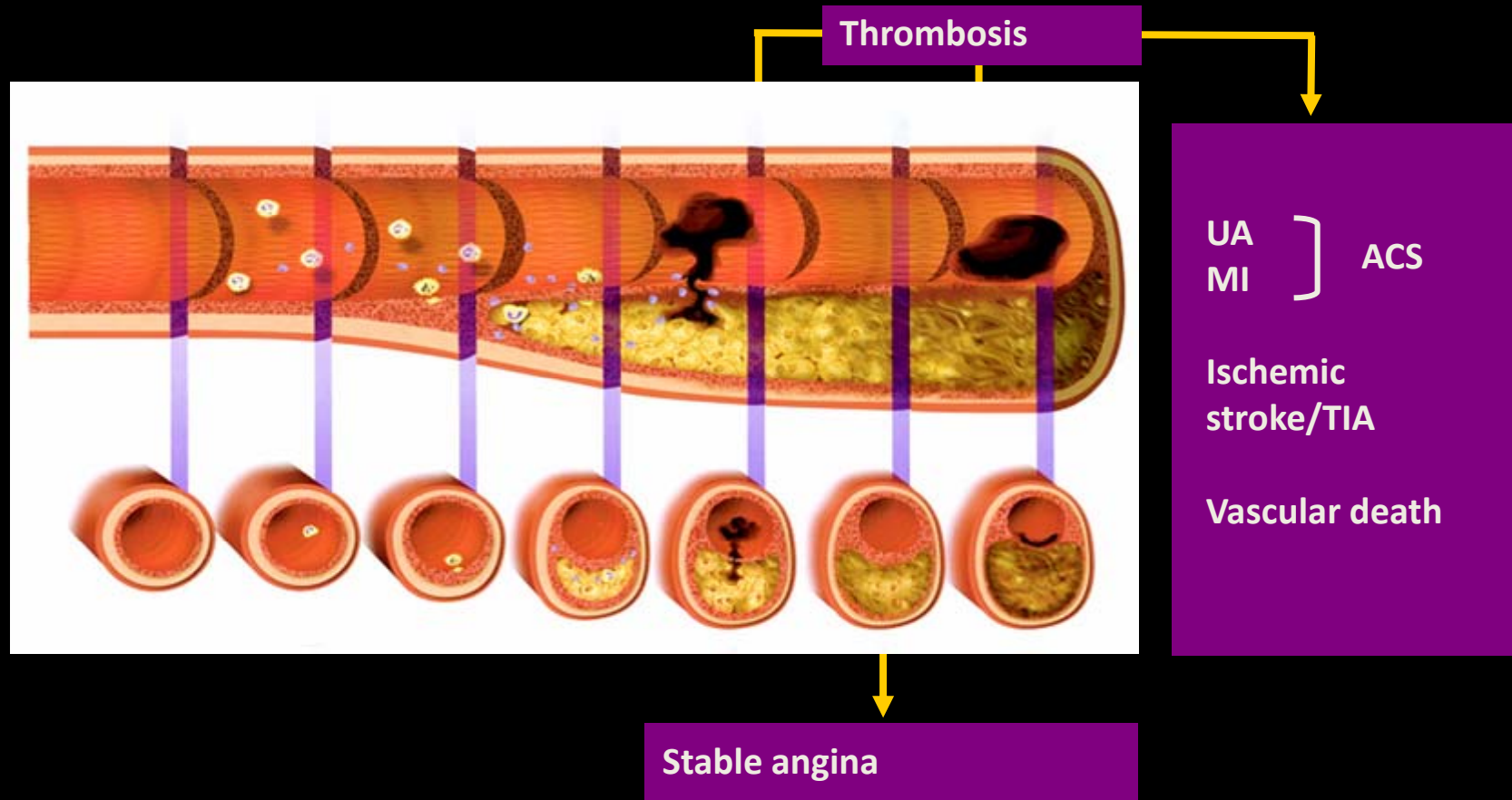
Stable angina

UA=unstable angina; MI=myocardial infarction;
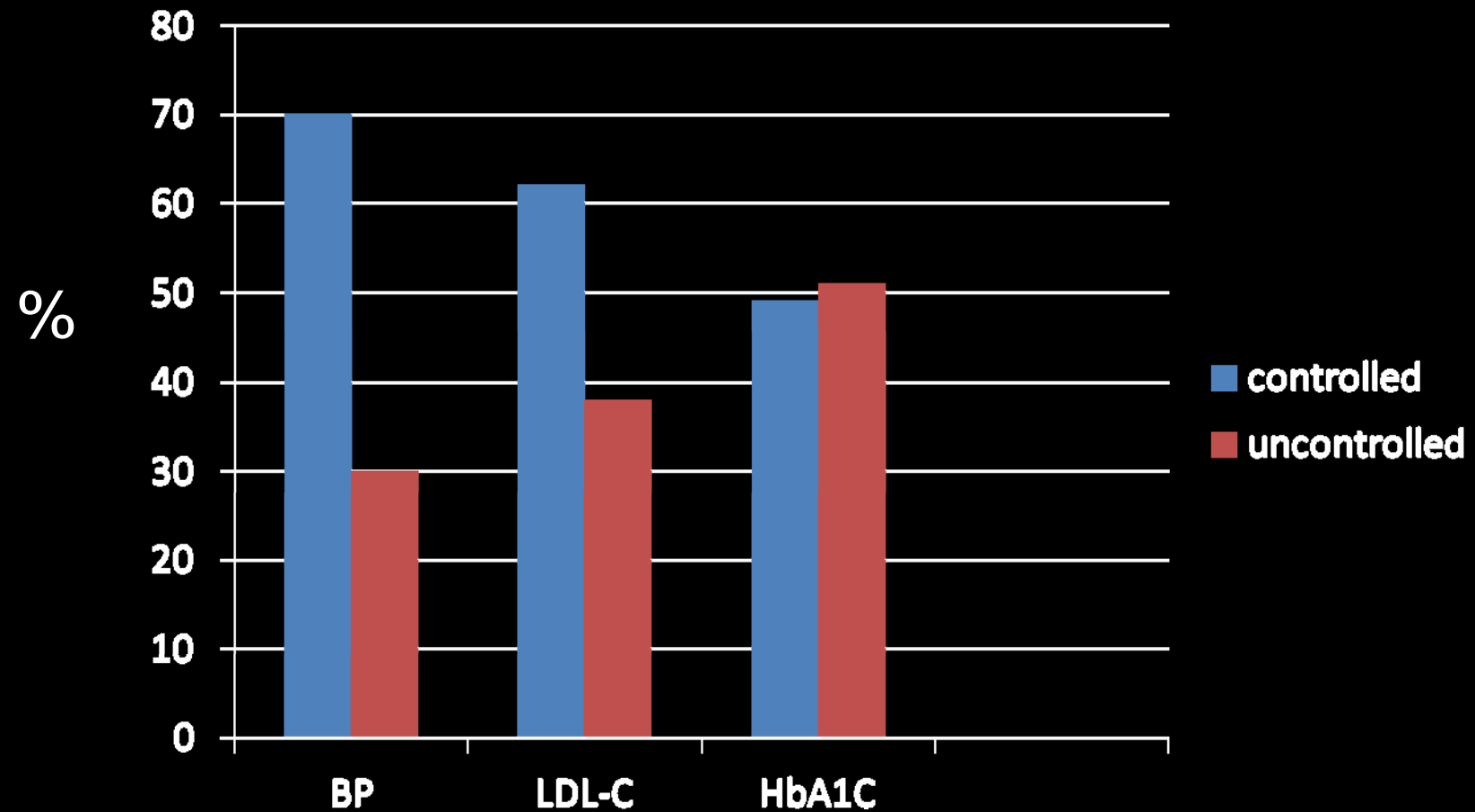ACS=acute coronary syndrome; TIA=transient ischemic attack

1. Adapted from Libby P. *Circulation* 2001; 104: 365–372.
2. Drouet L. *Cerebrovasc Dis* 2002; 13(Suppl 1): 1–6.

Triglyceride in ACS

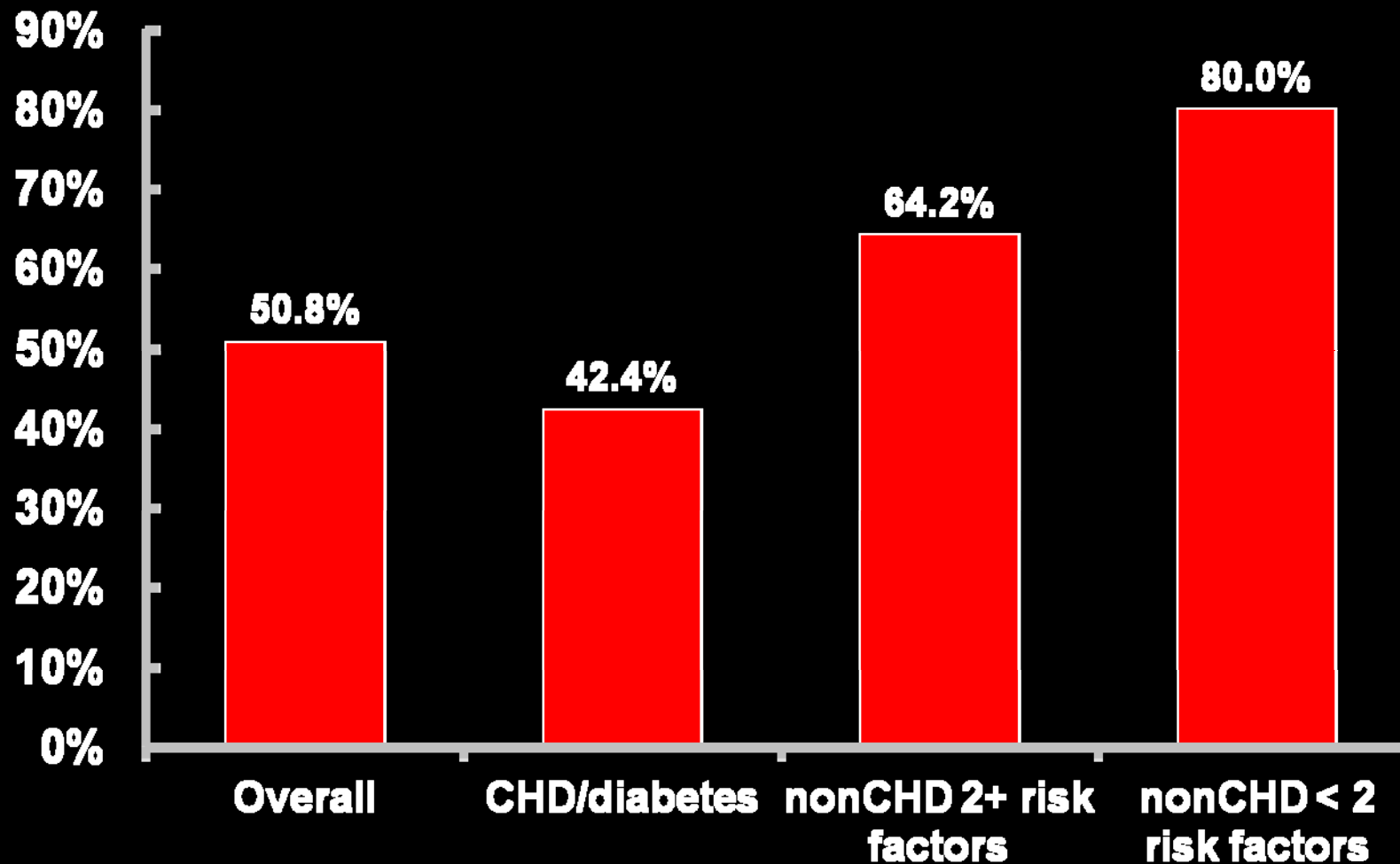| TG categories	Proportion (%)
< 150 mg/dl	66.6
150-249mg/d	26.0
>250 mg/dl	7.9

Risk factor control in CAD patients

Participating patients

- Planned for 10,000 patients
- Recruitment at each site
- 100- 500 patients per site
- Consecutive cases from each physician

Proportion Patients Attaining NCEP III Lipid Goals

Sub-studies of CORE-Thailand

- Hs-CRP and the incidence of cardiovascular events

- Platelet reactivity in patients treated with dual anti-platelet agents (aspirin, clopidogrel) and cardiovascular events

Hazard ratios (95% CI) for the association of risk factors with vascular death among 3318 Thais followed for an average of 12 years: EGAT

	Unadjusted	Adjusted[a]
Age (10 years)	3.7 (2.1, 6.5)	2.7 (1.5, 4.8)
Sex (male/female)	6.7 (1.6, 27.7)	2.6 (0.6, 11.1)
Body mass index (5 kg/m^2)	1.6 (1.1, 2.4)	1.0 (0.6, 1.6)
Systolic blood pressure (10 mmHg)[b]	1.7 (1.3, 2.2)	1.3 (1.0, 1.8)
Diastolic blood pressure (5 mmHg)[b]	1.7 (1.4, 2.2)	1.5 (1.1, 1.9)
Total cholesterol (1.0 mmol/l)[b]	1.1 (0.8, 1.7)	1.0 (0.7, 1.6)
HDL[c] cholesterol (0.2 mmol/l)	0.6 (0.5, 0.8)	0.7 (0.6, 0.9)
Diabetes[d] (yes/no)	5.3 (2.7, 10.2)	3.3 (1.6, 6.6)
Current smokers (yes/no)	2.8 (1.5, 5.2)	2.2 (1.1, 4.1)

LDL-C in Chiang Mai-ACS

LDL categories	Proportion (%)
< 100 mg/dl	39.9
101-130 mg/dl	29.9
131-160 mg/dl	17.8
>161 mg/dl	14.3

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

- Hospital: university hospital, tertiary care center, secondary care center