

Prevalence, Awareness and Treatment of Cardiovascular Risk Factors in Patients at High Risk of Atherothrombosis in Japan

— Results From Domestic Baseline Data of the REduction of Atherothrombosis for Continued Health (REACH) Registry —

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Background The REduction of Atherothrombosis for Continued Health (REACH) Registry is an international observational study of patients with, or at risk of, atherothrombotic disease. Japanese patients were analyzed to clarify national prevalence and treatment.

Methods and Results Almost 68,000 outpatients were recruited worldwide with 5,193 in Japan. Among the Japanese patients, 83.7% had established vascular disease (symptomatic) and 16.3% had risk factors only (asymptomatic). Of the symptomatic patients, 14.0% had atherothrombotic lesions in more than 1 vascular bed, with 0.8% having lesions in 3 areas: brain, heart, and peripheral arteries. The prevalence of additional atherothrombotic risk factors among symptomatic patients was independent of the vascular lesion. Obesity was recorded in 10.6% and 42.1% of patients according to the National Cholesterol Education Program and Japanese guidelines, respectively. Pharmacologic intervention for risk factors was inadequate: only 37.7% of diabetic patients received antidiabetic medication, 79.6% of hypertensive patients used antihypertensives, and 74.0% received antiplatelet agents. The use of statins (44.1%) and aspirin (54.7%) was less common than seen in REACH globally.

Conclusions Japanese patients enrolled in REACH share many similarities with the global population, but with some important differences. Long-term follow-up will determine the impact of these factors on the development of atherothrombotic events. (*Circ J* 2007; 71: 995–1003)

Key Words: Atherothrombosis; Japan; REACH; Risk factors

Atherothrombosis, caused by thrombotic occlusion of arteries¹ is a growing health concern, especially in the elderly population² Atherothrombosis may play a role in coronary artery disease (CAD), such as acute coronary syndromes, and cerebrovascular disease (CVD), such

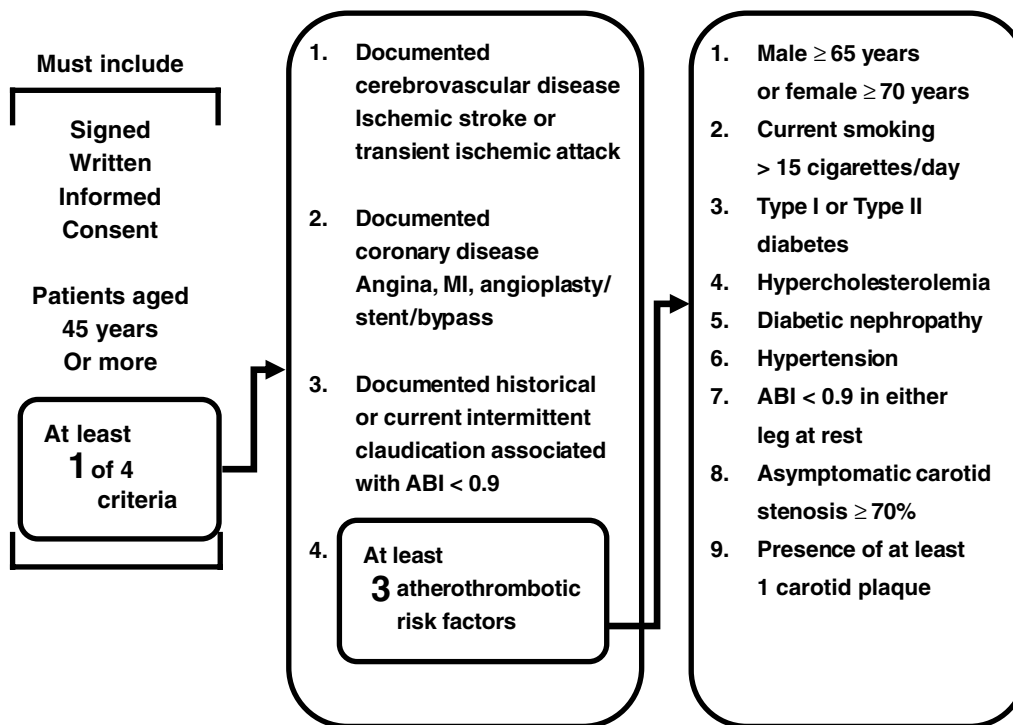
as ischemic stroke. According to the Japanese Ministry of Health Labor and Welfare (MHLW), there were 159,625 cardiac deaths and 129,055 deaths because of CVD in 2005, which make these the second and third most common causes of death in Japan, respectively.³ To develop improved strategies for the treatment and prevention of atherothrombotic disorders, which also includes peripheral arterial disease (PAD), greater understanding of their epidemiology is required. Clarification of the characteristics of atherothrombosis and its accompanying risk factors, verification of controllable risk factors, and subsequent validation of prevention and treatment strategies could then be determined.

Several Japan-wide cohort studies have been performed^{4–6} A regional cohort study, the Hisayama study, conducted in a similar manner to the Framingham Study^{7,8} provided important information on the specific characteristics of Japanese stroke patients.^{9,10} Likewise, the characteristics of Japanese CAD patients (JCAD) were clarified in the JCAD registry of CADs⁵ and in the NIPPON DATA80 studies.^{11,12} However, these regional or nationwide studies do not allow comparison between specific characteristics of patients in Japan and those in other regions of the world, as definitions of risk factors and disease may differ. In order to achieve this comparison, an international study using the same protocol and specifying inclusion criteria and definitions of

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MI, myocardial infarction; ABI, ankle brachial index.

Fig 1. Inclusion criteria.

disease is required. We have conducted the REduction of Atherothrombosis for Continued Health (REACH) Registry, an international observational study of patients with a history of established atherothrombotic disease, including CVD, CAD, and PAD, or asymptomatic patients who are at risk for these events. The study protocol¹³ and the patients' baseline characteristics worldwide¹⁴ have previously been described. The detailed baseline characteristics of Japanese patients recruited in the REACH Registry are presented here (ie, the patient characteristics at the time of entry into a long-term observational study).

Methods

Patients

The REACH Registry study design and inclusion criteria have been previously described.¹³ Briefly, patients were recruited if they were aged at least 45 years and with either established atherothrombotic disease (CAD, CVD, or PAD) or at high risk of atherothrombosis (Fig 1). Consecutive enrollment was used to avoid selection bias.¹³ Documented CAD was defined as a history of at least 1 of the following: stable angina, unstable angina, percutaneous coronary intervention, coronary artery bypass surgery, or myocardial infarction.¹³ A documented history of either transient cerebral ischemic attack (TIA) or symptomatic cerebral infarction defined CVD.¹³ PAD required documentation of intermittent claudication confirmed by an ankle-brachial index (ABI) less than 0.9 at the time of enrollment, a history of intermittent claudication with relevant intervention, or both.¹³

Risk factors for recruitment into the study are also defined in Fig 1. To be considered a risk factor for inclusion, systolic blood pressure ≥ 150 mmHg had to have occurred

for at least 3 months despite treatment. In order to meet the inclusion criteria, medical documentation or current pharmacologic treatment was required. Participation in clinical trials, hospitalization at the time of enrollment, and anticipated difficulty with long-term follow-up were reasons for exclusion. The internal review board at each participating institute approved the study protocol and patients gave written informed consent to participate. Worldwide, patients were recruited from December 2003 to June 2004. Patient recruitment in Japan started in August 2004 and ended in December 2004.

To reduce the risk of inclusion bias, patients from rural, suburban, and urban Japan were recruited by various specialty physicians (eg, general practitioner, cardiologist, neurologist, vascular surgeon, etc) from a variety of institutions (private clinic, community hospital, university hospital etc) (Fig 2). Physicians and their specialties were selected to be representative of healthcare usage by patients with or at risk of atherothrombotic conditions. The number of subjects was limited to 15 per physician.

Subjects will be followed for up to 4 years. Onset of atherothrombotic disease (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, and PAD) together with outcomes leading to hospitalization (including unstable angina, TIA, worsening PAD, and bleeding) will be recorded.

Baseline Data Collection

At the time of enrollment, demographic data such as age, gender, race, whether the patient was living alone, education, and work status were obtained, as well as physical data such as height, weight, waist circumference, and seated systolic and diastolic blood pressures. If available, laboratory data obtained in the previous 12 months, including serum

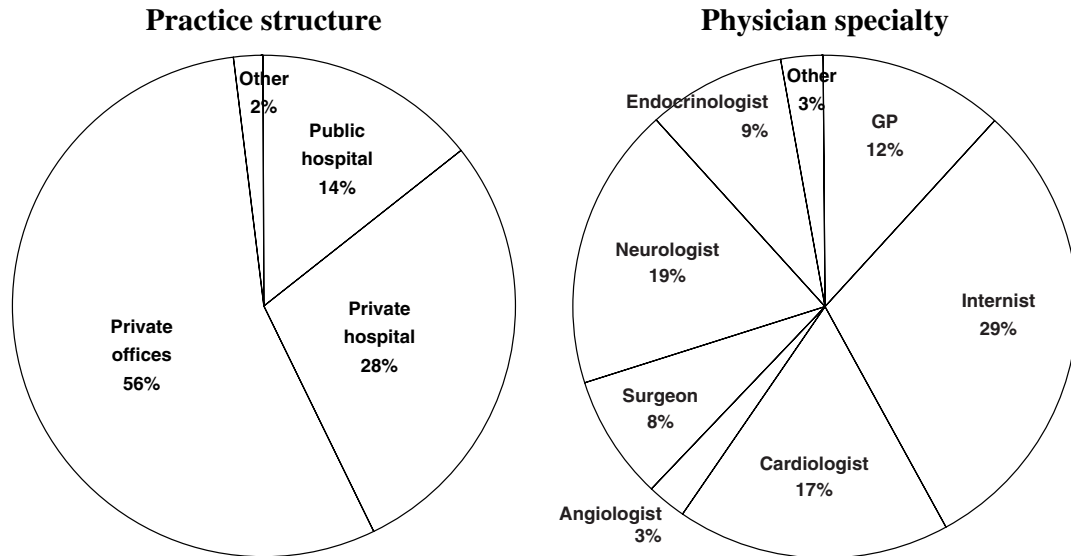


Fig 2. Type of participating sites and physician characteristics.

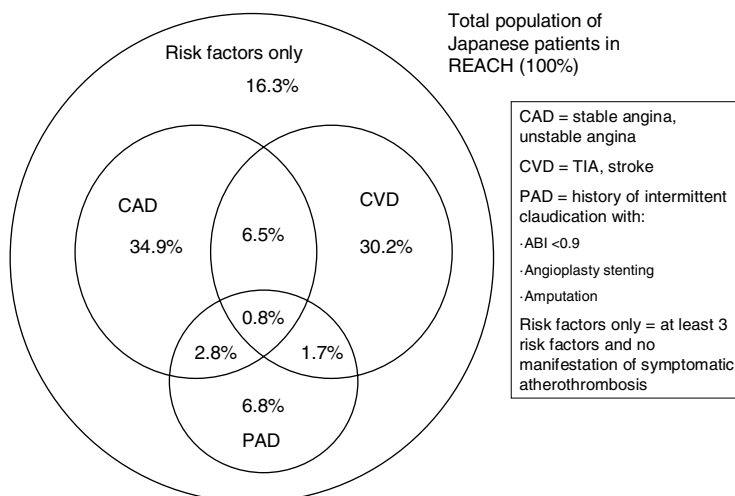


Fig 3. Profile of eligible Japanese patients. ABI, ankle brachial index; CAD, coronary artery disease; CVD, cardiovascular disease; PAD, peripheral arterial disease; REACH, REduction of Atherothrombosis for Continued Health; TIA, transient ischemic attack.

creatinine, fasting blood glucose, fasting total cholesterol, fasting triglyceride, high-density lipoprotein-cholesterol, and urine microalbumin, were also collected. Maximum carotid intima-media thickness and ABI were obtained in some patients. Medication data, including antiplatelet, lipid lowering, cardiovascular, and diabetes medications, were collected. Worldwide, similar definitions were used for a history of diabetes mellitus, hypertension or hypercholesterolemia, and for obesity¹³ and in Japan, the Japanese Society of Obesity definition for obesity was also applied.¹⁵

Data Analysis

Data quality management was conducted by visiting 10% of participating institutions. Auditing of baseline data was conducted in 4% of institutions that included at least 1 patient: 2% were randomly selected and 2% were selected based on issues arising from the institution and the number of missing values. Case reports of registered patients (100%) were examined for consistency and accuracy for all audited institutions.

Continuous variables are shown as mean and standard

deviation with categorical variables in terms of frequency and percentage. Categorical variables were compared using Pearson's χ^2 test and continuous variables using the t-test. Age and gender were controlled using a multiple logistic model in which the least square mean of each percentage value is calculated. When the 2-sided probability was <0.05, the result was considered statistically significant. Statistical analysis was conducted using SAS version 8 (SAS Institute Inc, Cary, NC, USA).

Results

More than 68,000 patients were recruited into the REACH Registry from 44 countries.¹⁴ In Japan, a total of 5,213 patients were enrolled from 390 sites. Duplicate registrations, consent withdrawals, and ineligible patients (registration during hospitalization [n=3] and insufficient risk factors [n=1]) resulted in 5,193 cases for baseline analysis.

Patient distribution by disease category (CAD, CVD and PAD) is shown in Fig 3. The majority of cases (83.7%) had

Table 1 Baseline Demographics of Japanese Subjects in REACH Registry

	Percentage of population					
	Total (n=5,193) [†]	Symptomatic (n=4,345)	CAD (n=2,334)	CVD (n=2,035)	PAD (n=627)	Risk factor only (n=848)
Age, mean (SD), years	70.3 (8.7)	70.2 (8.8)	69.7 (8.9)	70.9 (8.8)	72.2 (8.0)	70.7 (8.2)
Male	69.4	73.5	75.9	69.6	83.7	48.5
Diabetes [‡]	45.5	37.8	40.5	36.5	41.2	85.1
Hypertension [§]	70.8	70.3	68.0	74.4	77.8	73.4
Hypercholesterolemia	46.4	43.1	52.3	35.9	36.0	63.0
Obesity (Japanese guidelines) [‡]	42.1	42.7	44.1	42.1	41.5	39.2
Obesity (NCEP guidelines) [‡]	10.6	9.0	8.5	10.7	5.3	18.3
Overweight (BMI 25–29)	30.4	29.9	31.7	29.7	22.8	33.0
Obesity						
Class I (BMI 30–34)	3.7	3.3	3.3	3.3	1.6	6.1
Class II (BMI ≥35)	0.3	0.3	0.4	0.2	0	0.7
Smoker						
Former	45.4	50.1	53.5	45.8	61.0	21.4
Current	16.9	15.1	12.1	16.2	21.7	25.9

REACH, REduction of Atherothrombosis Continued Health; CAD, coronary artery disease; CVD, cardiovascular disease; PAD, peripheral arterial disease; NCEP, National Cholesterol Education Program; BMI, body mass index (weight [kg] divided by the square of height [m]).

[†]Because some patients with CAD, CVD or PAD were included in 2 or 3 categories, the total number of cases in the 3 categories exceeds 5,193.

[‡]Patients with type 1 or 2 diabetes who were being treated with hypoglycemic agents at the time of registration or the patients who had a history of diabetes.

[§]Patients who were treated with medications at the time of registration.

[‡]Men: waist circumference ≥85 cm, Women: waist circumference ≥90 cm.

[‡]Men: waist circumference ≥102 cm, Women: waist circumference ≥88 cm.

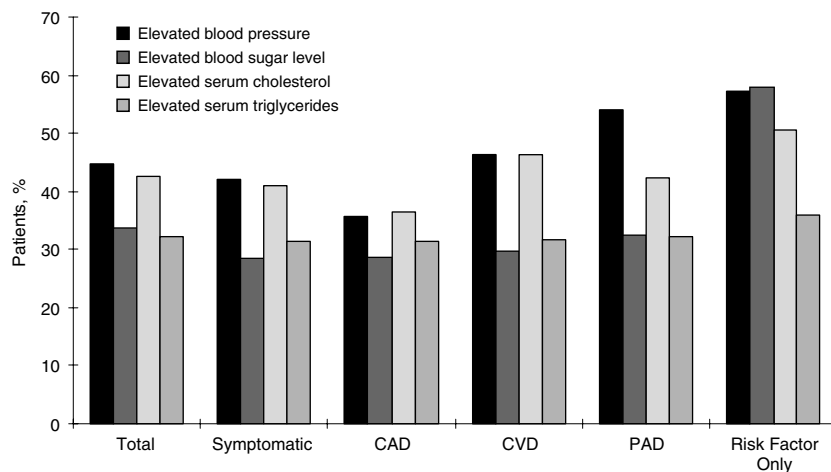


Fig 4. Percentage of patients (treated and untreated) with uncontrolled risk factors. CAD, coronary artery disease; CVD, cardiovascular disease; PAD, peripheral arterial disease.

established atherothrombotic disease (“symptomatic patients”), whereas only 16.3% had risk factors only (“asymptomatic patients”). Additionally, 11.8% of all patients (14.0% of symptomatic patients) had lesions in multiple areas. Only 0.8% of patients had lesions in the 3 vascular beds (brain, heart, and peripheral vessels).

Table 1 shows the baseline characteristics for all patients, by disease category. The majority of patients were male (69.4%). Hypertension was the most common comorbidity, which was diagnosed in 70.8% of all cases. Hypercholesterolemia (46.4%) and diabetes (45.5%) were also common, and the majority of patients were current (16.9%) or former smokers (45.4%). According to the National Cholesterol Education Program (NCEP) guidelines (waist circumference ≥102 cm for men and ≥88 cm for women), only 10.6% of patients were defined as obese; however, using the Japanese guidelines (waist circumference ≥85 cm for men

and ≥90 cm for women), this percentage increased to 42.1%.

Asymptomatic patients were more likely to be female, diabetic (85.1%), and have elevated serum cholesterol (63.0%), but were less likely to be past or current smokers, compared with the symptomatic patient population. Additionally, they were more likely to be classified as obese by NCEP standards but not by Japanese standards. Among symptomatic patients, hypercholesterolemia was most common in patients with CAD whereas hypertension was most common among patients with PAD.

To assess whether risk factors in symptomatic or asymptomatic patients were adequately controlled in Japan, the percentages of patients with elevated blood pressure (systolic pressure ≥140 mmHg, diastolic pressure ≥90 mmHg, or both),¹³ elevated blood sugar (≥126 mg/dl [6.99 mmol/L]), or elevated total serum cholesterol (≥200 mg/dl)¹⁶ and triglyceride levels (≥150 mg/dl) were calculated (Fig 4).

Table 2 Medication Use Among Japanese Patients in the REACH Registry by Atherothrombotic Event

	Percentage of population (%)				Risk factor only (n=848)
	Total (n=5,193) [†]	CAD (n=2,334)	CVD (n=2,035)	PAD (n=627)	
No. of patients with diagnosed hypertension or elevated blood pressure at initial examination	3,675	1,588	1,513	488	622
At least 1 antihypertensive agent	79.6	88.0	75.0	77.2	75.0
-blockers	18.8	31.1	11.6	12.9	9.4
ACE inhibitors	18.1	20.9	16.3	18.2	16.5
Diuretics	12.8	17.4	10.3	12.4	11.9
Calcium-channel blockers	55.9	57.9	55.4	57.4	55.4
Angiotensin II receptor blockers	32.0	31.2	32.8	30.8	36.4
Other antihypertensive agents	4.8	3.5	6.0	6.1	5.8
Antiplatelet therapy					
At least 1 antiplatelet agent	74.0	87.4	82.7	82.9	21.3
Acetylsalicylic acid	54.7	77.3	54.6	38.1	14.4
Other antiplatelet agents	31.9	28.8	41.9	62.0	8.0
Any 2 antiplatelet agents	12.5	18.6	13.2	17.2	1.1
Anticoagulant therapy	12.4	15.3	12.6	27.6	2.8
No. of patients with history of diabetes or elevated blood glucose at initial examination	2,365	946	743	258	722
At least 1 diabetes medication	37.7	30.6	28.6	35.1	81.5
Sulfonylureas	21.3	17.1	17.2	18.5	46.8
Biguanides	6.1	4.0	3.4	4.3	18.5
Insulin	11.1	9.3	7.2	12.1	24.9
Thiazolidinediones	3.0	2.4	2.5	1.8	6.7
Other diabetes medications	13.4	10.9	10.8	11.5	28.9
Nitrates	27.3	56.0	12.9	21.5	2.8
NSAIDs	3.0	2.6	3.5	3.7	3.0
Lipid-lowering therapy					
At least 1 lipid-lowering agent	50.8	57.9	39.2	44.2	66.0
Statin	44.1	52.1	33.7	32.9	58.1
Other lipid-lowering agents	9.8	10.2	7.7	14.4	10.6
No. of patients with PAD	627	186	127	627	0
PAD treatment drugs*	5.3	3.8	3.5	29.5	1.9

ACE, angiotensin-converting enzyme; NSAIDs, nonsteroidal antiinflammatory drugs. Other abbreviations see in Table 1.

*PAD drugs include prostaglandin drugs, argatroban and cilostazol (when used for intermittent claudication).

More than 40% of symptomatic patients were not being adequately controlled for blood pressure, serum cholesterol, or both. Compared with CAD patients, both CVD and PAD patients tended not to be well controlled for hypertension and elevated serum cholesterol.

The use of medications for the management of risk factors or for secondary prevention of atherothrombosis is shown in Table 2. Among patients with elevated blood pressure, 79.6% were being treated with antihypertensive agents. Calcium-channel blockers were the most frequently prescribed class of antihypertensive. Overall, 74.0% of patients were treated with antiplatelet agents. The proportion of patients treated with at least 1 antiplatelet agent was high, exceeding 80% in all categories of symptomatic patients, compared with only 21.3% in the asymptomatic group. Among the symptomatic patients, the use of aspirin was greatest among patients with CAD (77.3%) and least among patients with PAD (38.1%), who were more likely to be treated with anticoagulants. Treatment for diabetes was much less common in patients with a history of diabetes or elevated blood glucose levels who were in the symptomatic subset compared with those in the asymptomatic group (30.6% vs 81.5%, respectively). Symptomatic patients were also less likely to have adequate glucose control than the asymptomatic patients (40% controlled vs 72% controlled, respectively). Lipid-lowering agents were prescribed to most asymptomatic patients, as well as to those with a history of CAD; however, the majority of CVD

and PAD patients did not receive such medications.

Regarding medication use among patients according to the specialty of their treating physician (Table 3), antihypertensive agents were frequently prescribed regardless of physician specialty. Antiplatelet agents and lipid-lowering therapies were also commonly prescribed, but with somewhat more variation between specialties.

Discussion

The REACH Registry is a large-scale global survey of patients at risk of atherothrombotic events, including patients with a past history of atherothrombotic disease (CAD, CVD, and PAD) and those at high risk for a first event. In the global baseline data it was noted that atherothrombotic patients throughout the world had similar risk profiles, with a history of hypertension (81.8%), hypercholesterolemia (72.4%), diabetes (44.3%), atherothrombosis in more than 1 vascular bed (15.9%), and obesity (46%).¹⁴ Patients were generally undertreated with statins (69.4% overall), antiplatelet agents (78.6% overall), and other evidence-based risk reduction therapies.¹⁴ There was substantial current use of tobacco (14.4%) in patients with established disease.¹⁴

Among patients registered in Japan, the results were comparable with those from the global survey.¹⁴ Patients recruited with documented atherothrombotic disease had a history of hypertension (70.3%), hypercholesterolemia (43.1%), diabetes (37.8%), and current smoking (15.1%).

Table 3 Medication Use Among Japanese Patients in the REACH Registry by Physician Specialty

	Patient population by physician specialty (%)							
	GP (n=600)	Internist (n=1,529)	Cardiologist (n=926)	Angiologist (n=138)	Surgeon (n=438)	Neurologist (n=961)	Endocrinologist (n=448)	Other (n=138)
No. of physicians in specialty	47	116	68	10	31	72	34	11
At least 1 antihypertensive agent	82.7	82.3	89.6	92.0	74.4	69.2	71.2	76.1
-blockers	18.7	16.9	36.0	41.3	11.2	7.9	12.1	24.6
ACE inhibitors	18.7	18.1	26.7	23.9	13.7	13.8	13.2	11.6
Diuretics	11.7	15.6	15.9	16.7	12.6	6.1	10.0	21.0
Calcium-channel blockers	57.3	59.1	56.6	64.5	56.2	51.6	50.5	51.5
Angiotensin II receptor blockers	31.0	35.5	30.2	34.1	27.6	29.8	37.1	20.3
Other antihypertensive agents	3.0	6.2	2.7	8.0	4.3	5.6	4.5	5.8
Antiplatelet therapy								
At least 1 antiplatelet agent	69.5	66.8	86.5	84.1	80.6	83.8	45.8	83.3
Acetylsalicylic acid	55.2	51.9	80.0	61.6	33.8	52.2	31.5	67.4
Other antiplatelet agents	25.0	27.3	23.8	32.6	61.2	42.6	23.4	26.1
Any 2 antiplatelet agents	10.7	12.3	17.3	10.1	14.4	11.0	9.2	10.1
Anticoagulant	7.8	10.9	13.1	15.2	30.6	8.6	5.6	34.8
At least 1 diabetes medication	35.8	46.5	26.4	30.4	23.1	20.1	91.3	29.0
Sulfonylureas	24.3	25.8	15.4	15.2	9.8	12.9	46.2	19.6
Biguanides	5.7	9.0	2.6	2.9	2.5	3.1	16.7	2.9
Insulin	6.1	14.9	5.6	8.0	8.7	3.1	37.3	10.1
Thiazolidinediones	2.1	5.4	1.5	2.9	1.1	1.3	4.7	2.2
Other diabetes medications	11.8	15.7	11.3	13.0	7.8	7.8	30.8	12.3
Nitrates	27.0	29.3	49.0	34.8	25.1	7.7	13.8	41.3
NSAIDs	4.0	2.8	1.6	1.5	3.4	3.9	2.2	5.1
Lipid-lowering therapy								
At least 1 lipid-lowering agents	52.3	54.4	60.7	61.6	39.5	33.6	65.0	39.1
Statin	46.0	46.3	55.8	55.8	29.7	28.5	58.3	32.6
Other lipid-lowering agents	8.5	11.1	9.2	8.0	11.9	7.0	12.5	10.9
PAD treatment drugs*	2.8	3.5	2.6	2.9	26.5	2.2	4.2	15.9

Abbreviations see in Tables 1,2.

*PAD drugs include prostaglandin drugs, argatroban and cilostazol (when used for intermittent claudication).

In the REACH Registry, patients were recruited by the participating physician. Therefore, these results may not directly reflect the prevalence of disease in the Japanese population. Many patients recruited in Japan (39.2%) had documented CVD, a greater proportion than that observed in the global REACH cohort (27.8%),¹⁴ which supports the notion that the characteristics of atherothrombosis in Japanese people may not be the same as those in other countries. It should be noted that neurologists made up a greater proportion of participating physicians in Japan compared with other regions participating in the REACH Registry.¹³ The proportion of recruiting physicians of different specialties in each participating country was chosen to reflect the local prevalence of different atherothrombotic conditions.¹³ According to MHLW statistics, the prevalence of CAD in Japan in 2002 was 911,000 and for CVD it was 1,374,000.³ The prevalence of CVD in Japanese patients in the REACH study is in agreement with the comparative meta-analysis of a regional cohort study,¹⁷ which suggests that the composition of recruiting physicians in REACH-Japan is representative of the local healthcare environment.

A history of atherothrombosis in more than 1 vascular bed was found in 13.8% of Japanese patients, which is similar to that seen in the overall REACH population (15.9%).¹⁴ This demonstrates the diffuse nature of atherothrombosis and implies that it may be best treated as a systemic disease.

Using the global standard of BMI >30, only 3.7% of patients were determined to be obese in Japan, which was the lowest percentage in the world.¹⁴ Using waist circumference, only 10.6% of the Japanese patients were designated as obese using the global NCEP criteria. However, excess body fat may be better defined based on country-specific guidelines that consider the physiognomy of the indigenous

population. Therefore, we applied the Japanese criteria for obesity to the Japanese patients recruited into the REACH Registry and using these criteria, 42.1% of Japanese patients were classified as obese, which is close to the value of 46% reported globally.¹⁴ The utility of these different markers for obesity in the Japanese population may become clearer when they are analyzed against the data for event rates at the end of the study.

It has been hypothesized that a diet rich in salt, which is common in Japan, may lead to an increased risk of hypertension and CVD.¹⁸ The consecutive recruitment of patients in REACH was expected to enroll a cohort that accurately represents the general Japanese population of patients with atherothrombosis. By extrapolation from the general Japanese population, the patients in REACH would be expected to have a relatively high-salt diet compared with patients enrolled from other countries. However, the prevalence of hypertension among Japanese patients in REACH (70.8%) was somewhat lower than that previously described in the global cohort (81.8%).¹⁴ which could be linked to the rate of obesity. However, in contrast, the prevalence of CVD in Japanese patients (39.2%) was higher than that in the global cohort (27.8%).¹⁴ Detailed analysis of follow-up data in the REACH Registry may help to elucidate the reasons for a higher prevalence of CVD among Japanese patients with atherothrombosis.

Japanese physicians prescribe antihypertensive agents differently from physicians elsewhere. Calcium-channel blockers (55.9%) and angiotensin II receptor blockers (32.0%) were prescribed more frequently than in the global population (37.2% and 25.4%, respectively),¹⁴ while prescription of -blockers (18.8%), diuretics (12.8%), and angiotensin-converting enzyme inhibitors were less com-

monly used (cf. 48.9%, 44.0%, and 48.2%, respectively). This unique way of prescribing antihypertensives was mirrored in the asymptomatic population. The use of antihypertensives (75.0%) in the asymptomatic group in Japan was substantially less than that seen globally (96.7%)¹⁴ despite the fact that a majority of asymptomatic patients had inadequately controlled hypertension (almost 60%). The risk of spastic angina, believed to be more common in Japan, may dissuade physicians from choosing β -blockers as first-line antihypertensive agents!⁹ However, we observed that cardiologists use β -blockers more frequently than other specialists, suggesting that the issue of spastic angina may not be a real concern. Differences in prescribing practice are also likely to reflect differences in the type of patient that each specialist sees.

An important difference between Japan and the rest of the world is also demonstrated in the choice of antiplatelet agents:²⁰ Among asymptomatic patients, 21.3% were treated with at least one antiplatelet agent in Japan compared with 53.9% worldwide. This may be related to a lack of evidence in Japanese patients for the use of antiplatelet agents for primary prevention of atherothrombotic disease!²¹ Furthermore, only 54.7% of Japanese symptomatic patients were treated with aspirin compared with 67.4% globally!¹⁴ Again there were differences in prescribing among recruiting physicians, with aspirin more likely to be prescribed by cardiologists (80.0%) compared with vascular surgeons (33.8%). A greater proportion of other antiplatelet agents was used in Japan (31.1%) compared with global use (24.7%).¹⁴ These included ticlopidine and cilostazol but not clopidogrel, which had not yet been approved in Japan at the time of study recruitment. The latter has demonstrated efficacy advantages over aspirin in global studies of patients with atherothrombosis²² (CAPRIE), and a safety advantage over ticlopidine in stroke patients (Plavix Japan Prescribing Information). Therefore, the use of non-aspirin antiplatelet agents in Japan might be expected to increase over time.

Patterns of glycemic control and the use of appropriate diabetic medications differed between patients with a history of atherothrombosis and those only at risk. Among diabetic patients in the symptomatic group, approximately 30% were being treated, but more than 70% achieved adequate glycemic control. This may be attributed to increased patient adherence to appropriate diet and exercise regimens following an atherothrombotic event or to the type of diabetic patients recruited. Conversely, more than 80% of diabetic patients in the asymptomatic cohort were prescribed at least 1 medication for diabetes, but nearly 60% had elevated fasting glucose. Underuse of diabetes medications and inadequate glycemic control at baseline may be attributed to the detection of previously unrecognized fasting hyperglycemia, suggesting that improvements may be needed in screening and treating diabetes for patients who have had, or are at risk for, an atherothrombotic event.

With regard to the choice of diabetes medication, a much smaller percentage of patients (37.7%) in Japan was treated with at least 1 agent compared with the global population (85.9%).¹⁴ From a global perspective, sulfonylureas and biguanides were used with a similar frequency (42.7% and 40.0%, respectively)¹⁴ but in Japan, there is a strong preference for sulfonylureas (21.3% compared with 6.1% of biguanides). This may reflect the physiology of diabetes in Japanese patients, in whom deficiencies in insulin secretion are more common than insulin resistance. Insulin use in Japan was higher in the asymptomatic (24.9%) than in the

symptomatic population (11.1%), whereas in the global population these rates were similar (22.9% and 25.7%, respectively).¹⁴

Lipid-lowering agents, including statins (50.8%), were prescribed much less frequently in Japan compared with the worldwide cohort (75.2%).¹⁴ Despite the insufficient therapeutic effect indicated by elevated cholesterol (43%) at baseline, these results were similar to those from other areas of the world!¹⁴ A higher percentage of patients in the asymptomatic group were treated with lipid-lowering agents (66.0%), yet a much larger proportion of these patients (almost 60%) were poorly controlled.

In conclusion, we have examined the baseline data from a subgroup of 5,193 Japanese patients enrolled in the international REACH Registry. Although the overall profiles were similar in the Japanese and worldwide populations, the proportion of obese patients was lower in Japan, but more patients had CVD. Use of lipid-lowering agents and diabetes medication was lower in Japan, although the overall rate of insufficient medication use was similar. As seen in the global population, atherothrombotic risk factors for many patients in Japan are undertreated and undercontrolled. During the follow-up phase of the REACH Registry, we will assess the impact of risk factors on the rate of subsequent morbidity and mortality from atherothrombotic disease in a Japanese population. This information may provide evidence that can be used to modify existing treatment guidelines in order to improve the health of Japanese patients who are at risk of atherothrombotic events.

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Appendix 1

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