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DOI: [10.1159/000087008](https://doi.org/10.1159/000087008)**Atherothrombosis and Stroke –
A Lot More to Know!**

Announcement of an International, Prospective Registry in
Subjects at Risk of Atherothrombotic Events in an Outpatient
Setting – The REACH Registry

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Atherothrombosis is the driving force underlying myocardial infarction (MI), peripheral arterial disease (PAD) and stroke. There are still significant gaps in our knowledge of the etiology and risk factors of cardiovascular disease, and in particular stroke, especially with respect to the relative importance of disease risk factors. Stroke risk factors have mainly been determined from the examination of composite outcome measures in cardiovascular clinical studies. For reasons of increased statistical power, stroke, MI and vascular death are often grouped together. It is then commonly assumed that risk factors have the same effect on the various manifestations of atherothrombosis. However, this may not hold entirely true. Blood pressure for instance is a more relevant risk factor for stroke whereas cholesterol levels have a higher impact on coronary vascular events [1].

Furthermore, the influence of many of the ‘new’ risk factors has not been properly evaluated for ischemic stroke; body mass index (BMI), obesity, diabetes, metabolic syndrome, chronic heart failure, chronic renal failure, ankle brachial index and C-reactive protein are all considered risk factors mainly by deduction from combined endpoints from cardiovascular studies. For example, BMI has been identified as a stroke risk factor in men [2] but no data are available in women. Abdominal obesity, measured as waist circumference, has been shown to be associated with insulin resistance, hyperinsulinemia and glucose intolerance [3] and might prove to be an easily assessable risk factor. However, studies of the associa-

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Table 1. Inclusion criteria for the REACH Registry

Subjects aged 45 years or older with at least one of the following four criteria

- 1 Documented coronary disease (one or more criteria must apply)
 - Previous myocardial infarction
 - History of coronary angioplasty/stenting
 - History of coronary artery bypass graft
 - Stable angina
 - History of unstable angina
- 2 Documented cerebrovascular disease (one or both criteria must apply)
 - Previous ischemic stroke
 - Previous transient ischemic attack
- 3 Documented symptomatic peripheral arterial disease (one or both criteria must apply)
 - Current intermittent claudication with Ankle Brachial Index <0.9
 - History of intermittent claudication together with previous related intervention (angioplasty, bypass graft, other vascular intervention including amputation)
- 4 Combination of at least three atherothrombotic risk factors
 - Systolic blood pressure ≥ 150 mm Hg despite therapy for at least 3 months
 - Known presence of at least one carotid plaque (as evidenced by intima-media thickness measured by ultrasonography and exceeding twice that of neighboring sites)
 - Known asymptomatic carotid stenosis ($\geq 70\%$)
 - Hypercholesterolemia currently treated with medication
 - Type I or II diabetes currently treated with hypoglycemic agents
 - Evidence of diabetic nephropathy (microalbuminuria ≥ 30 $\mu\text{g/ml}$)
 - Known Ankle Brachial Index <0.9
 - Current smoking >15 cigarettes per day
 - Male ≥ 65 years or female ≥ 70 years

tion with stroke are still pending. More epidemiological data are needed that focus on the atherothrombotic risk of patients and seek to establish the influence of classical and ‘new’ risk factors on cerebrovascular disease.

We herewith announce the start of a prospective registry in subjects at high risk of atherothrombotic events. The REACH (Reduction of Atherothrombosis for Continued Health) Registry is an international study that has recruited 67,888 subjects in 44 countries

across six major regions. Participants are aged 45 years or older and have at least three atherothrombotic risk factors or a documented cerebrovascular or coronary event or existing PAD (table 1). Recruitment has focused on general practice, although some hospital-based physicians have been recruited to ensure a broad cross-section of physicians who treat patients with atherothrombosis. No hospitalized patients or patients participating in a clinical trial were recruited into the study. Patients were recruited consecutively at each site to ensure a representative study population. The recruitment phase of the Registry is completed and follow-up data are collected.

Medical history, risk factors, demographic information, employment status, risk factors and chronic medical treatments have been recorded at baseline along with a physician profile. During the follow-up period of up to 2 years duration, a record will be kept of any clinical events occurring, any causes of hospitalization or death, any chronic medical treatment, any sick leave and any changes to the employment status of the participant.

Aspects of Stroke Epidemiology that Might Be Elucidated by the REACH Registry

Influence of Multiple Risk Factors

The REACH Registry will study the dependency of stroke incidence from the risk factor profile and will explore the risk of stroke in other cohorts. Age is the most powerful independent risk factor for stroke and with increasing life expectancy the risk of stroke increases greatly. Data on age-dependent stroke incidence rates, country-specific subgroup evaluations, world- and Europe-wide incidence values of 'at-risk patients' in the high-risk REACH population will be assessed. It is very likely that stroke management is influenced by patient age. The REACH Registry will deliver data upon age-dependent rates of hospitalization for stroke and show how current treatment guidelines [4] of secondary stroke prevention are followed depending on age.

Gender differences in the management of patients with ischemic heart disease and stroke are well known [5, 6]. Women who develop strokes are older, have worse pre-stroke Rankin scores, more risk factors, receive less aggressive therapy, and undergo fewer diagnostic procedures. The REACH Registry will deliver data on the gender-specific incidence rates of stroke, prevalence of specific risk factors, pre-stroke functional status and medication.

Socioeconomic Status as a Risk Factor

It is likely that socioeconomic status influences the prevalence of stroke risk factors and disease management. Insurance systems differ between nations and across social classes. Education is the most important determinant of socioeconomic status. The REACH Registry will assess education and employment status and new data on the incidence of risk factors; differences in preventive medicine depending on socioeconomic status will be analyzed.

Outcome by Region/Country

The REACH Registry has recruited patients in 44 countries located in North America, Latin America, Europe, Australia, Asia and the Middle East. Outcome event rates will be evaluated by country providing valuable information on regional influences on stroke incidence and risk.

Health Economics

Stroke is the second leading cause of death worldwide. There are conflicting data on the cause of death in stroke patients (a further stroke or MI). Since stroke accounts for the majority of nursing home and hospital-bed days, the information expected from the REACH Registry on the cause of death and the disability after stroke will be important from the perspective of health economics [7].

Summary and Conclusions

The REACH Registry will be the first study to provide prospective data across the spectrum of subjects at high risk for atherothrombosis on a basis in a real-world setting. The REACH Registry will provide information on secondary events in a stroke and TIA population and can be expected to provide a wealth of interesting data on atherothrombosis burden, stroke prevention and epidemiology, which will, in due course, be made available in the published literature.

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