

# Small Changes in Type 2 Yield Big Rewards

BY MICHELE G. SULLIVAN

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

LISBON – Even small changes in hemoglobin A<sub>1c</sub> and blood pressure could significantly reduce the risk of heart attack, stroke, and other cardiovascular complications in people who have type 2 diabetes, according to the findings of a population-based observational study of nearly 6,000 patients.

A 0.5% decrease in HbA<sub>1c</sub> and a 10-mm Hg decrease in systolic blood pressure could avert 10% of such events over the course of 5 years, Dr. Edith Heintjes said at the annual meeting. Greater changes could reduce cardiovascular events by as much as 21%, said Dr. Heintjes of the PHARMO Institute for Drug Research, Utrecht, the Netherlands.

Although Dr. Heintjes' study on population attributable risk was theoretical, it still adds weight to the emerging theory that small changes can make a big difference to the health of people with type 2 diabetes.

"Even when we examined only modest incremental reductions, which could be achieved in the clinical setting, we found the possibility of significant benefit," she said.

Those patients who had the greatest risk factors – elevated HbA<sub>1c</sub>, high blood pressure, and higher body mass index – stand to gain the most when they improve those factors, she said.

Dr. Heintjes' analysis included 5,841 Dutch patients with a diagnosis of type 2 diabetes for at least 2 years.

## VITALS

**Major Finding:** Reducing HbA<sub>1c</sub>, blood pressure, and weight could avert up to 21% of cardiovascular events in patients with type 2 diabetes.

**Data Source:** A population-based observational study comprising 5,841 patients.

**Disclosures:** Dr. Heintjes reported having no conflicts of interest. Her employer, PHARMO, however, receives funding from numerous pharmaceutical companies, including Astra Zeneca, which sponsored the current study.

The patients were all taking some form of treatment – oral medications, insulin, or both – for at least 6 months to be included in the study.

After examining both baseline data and 5-year outcomes, Dr. Heintjes was able to extrapolate how improvements in the three risk factors might impact the expected number of cardiovascular events.

Patient data were drawn from the PHARMO record linkage system, which includes community pharmaceutical dispensing information, laboratory information, national hospitalization information, and statistics from the Dutch national diabetes monitoring program.

Patients were treated with the aim of achieving the country's national targets: an HbA<sub>1c</sub> of below 7%, a systolic blood pressure of 140 mm Hg or lower, and a body mass index of 25 kg/m<sup>2</sup> or less.

At baseline, the patients' average age was 66 years. The average HbA<sub>1c</sub> was 7%; systolic blood pressure 149 mm Hg, and body mass index, 29.5 kg/m<sup>2</sup>.

Most of the patients (92%) were taking only oral medications. The rest of

them were also taking insulin.

Some cardiovascular morbidity was already present in the group, including peripheral artery disease (0.5%), renal impairment (11%), neuropathy (51%), and retinopathy (7%). About half of the group (45%) had a family history of cardiovascular disease.

Dr. Heintjes divided the group according to the number of risk factors each patient exhibited. A quarter (24%) had just one elevated risk factor; 47% had two elevated risk factors, and 26% had elevations in all three risk factors.

A multivariable analysis allowed her to extrapolate that 796 cardiovascular events (heart attack, ischemic heart disease, stroke, and chronic heart failure) would occur if all of the patients were followed for 5 years.

If every patient in this population were able to correct each one of the risk factors to the national recommendations, she said, 687 events would occur – a 14% decrease. Correcting HbA<sub>1c</sub> and blood pressure accounted for this change, she said; changing BMI did nothing to increase the benefit.

Theoretically, she said, patients with the most risk factors would reap the

greatest benefit. The 24% with one elevated risk factor would experience a 5% reduction in cardiovascular events, while those with all three elevated risk factors, upon correcting them, would see a 21% reduction.

With regard to the group's baseline measurements, correcting to national Dutch standards would mean an average HbA<sub>1c</sub> reduction of 0.8%, a 26-mm Hg reduction in systolic blood pressure, and a weight loss of 16 kg (equivalent to a BMI decrease of 5.7 kg/m<sup>2</sup>).

However, Dr. Heintjes said, it might not be realistic to expect such changes.

Her second analysis explored the improvements that could arise from smaller changes: a 0.5% reduction in HbA<sub>1c</sub>, a 10-mm Hg reduction in systolic blood pressure, and a 10% reduction in total body weight (2.6 kg/m<sup>2</sup> decrease in BMI).

"With this analysis, we saw in the overall population that 6% of the risk could be averted," she said. Among those patients in the subpopulation

with three risk factors, applying the smaller changes could cut the number of events by 10%.

It's not exactly clear how the results can change clinical practice, Dr. Heintjes acknowledged.

"But this does allow us to understand how small changes can translate into bigger benefits for people with type 2 diabetes," she said. ■

**A 0.5% decrease in HbA<sub>1c</sub> and a 10-mm Hg decrease in systolic blood pressure could avert 10% of cardiovascular complications over the course of 5 years.**

## Stroke Risk Surges After 10 Years in Diabetes Patients

BY BETSY BATES

FROM THE ANNUAL MEETING OF THE AMERICAN NEUROLOGICAL ASSOCIATION

SAN DIEGO – The risk of ischemic stroke more than triples in patients with a 10-year history of diabetes, according to results of the population-based

**'Diabetes, like hypertension and all of the other risk factors for cardiovascular disease, takes a while to really cause big damage. ... You have a lot of time for intervention.'**

Northern Manhattan Study.

Ischemic stroke has long been associated with diabetes, but a large, longitudinal study enabled investigators to explore how risk changes over time, Dr. Julio R. Vieira said at the meeting.

Columbia University researchers followed 3,298 multi-ethnic patients who had no prior history of stroke, assessing for diabetes at baseline and annually, beginning in 1993.

At baseline, the mean age of subjects was 69 years (range, 59-79). More than half were Hispanic, with 24% black and 21% white.

Initially, 717 patients (22%) had diabetes and 338 (10%) developed new-onset diabetes over the course of the study.

During a median of 9 years of follow-up, 244 patients were diagnosed with ischemic stroke.

In Cox proportional hazards models, patients with diabetes at baseline faced a 2.5-fold increased risk of having an ischemic stroke during the study period. Among those patients and those who developed de

novo diabetes, the risk of ischemic stroke rose over time.

Risk was elevated 70% among patients with diabetes for 5 years or less, 80% for those with a 5- to 10-year history of diabetes, and 3.3-fold for those with at least a 10-year history of the disease.

The majority of patients in the study had type 2 diabetes, Dr. Vieira said in an interview following his presentation during a cardiovascular group session at the meeting.

Although risk of ischemic stroke was present from the start in diabetic patients, it did not triple for a decade, he stressed in the interview.

"Diabetes, like hypertension and all of the other risk factors for cardiovascular disease, takes a while to really cause big damage," he said.

"That's exactly what we're seeing here."

To Dr. Vieira, a research fellow at the Neurological Insti-

## VITALS

**Major Finding:** Study participants with at least a 10-year history of diabetes had more than three times greater risk for stroke than did participants without diabetes.

**Data Source:** The Northern Manhattan Study, a population-based, longitudinal study of 3,298 people.

**Disclosures:** Dr. Vieira and all coinvestigators, except one, had no relevant disclosures. The principal investigator of the study, Dr. Mitchell Elkind, reported serving as a consultant to Bristol-Myers Squibb and Tethys Bioscience; serving on speakers' bureaus for Boehringer-Ingelheim, Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, and Genentech; and receiving research support from diaDexus, Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, and the National Institute for Neurological Disorders and Stroke (NINDS). He also has given expert testimony on behalf of Novartis and GlaxoSmithKline for stroke litigation. The study is supported by a grant from NINDS.

tute of New York at Columbia University, the message for physicians and patients alike is, "You have a lot of time for intervention."

He said that in his own experience, warning diabetic patients of impending problems with their eyes, hearts, or extremities does not always seem

to get their attention.

Perhaps it would be more sobering to tell them that they have 10 years to get the disease under control, or face a tripling of their risk of a potentially fatal or disabling stroke, he speculated.

"Maybe people will get the message," he said. ■