Diabetes prevention interventions show long-term benefits

A long-term follow-up study has shown that lifestyle interventions to prevent diabetes can exert effects for up to 14 years after the active intervention.

Specialists at centres in Beijing and Da Qing, China, in Atlanta and Phoenix, USA, and in Geneva, Switzerland, followed up people who took part in the Da Qing Diabetes Prevention Study. In this 6-year study, which began in 1986, a total of 576 adults with impaired glucose tolerance (IGT) were randomly assigned by clinic to either one of three lifestyle intervention groups (diet alone, exercise alone, or diet plus exercise; all with associated counselling at regular intervals) or a control group.

In the active intervention groups, the incidence of type 2 diabetes was reduced by 31-46%, compared with the control group.

For the new study, the researchers obtained follow-up information on 563 patients relating to a diabetes diagnosis, 542 patients relating to first cardiovascular disease (CVD) events, and 568 patients relating to mortality. The three intervention groups in the initial study were combined into one group for the new analysis.

At the end of the original 6-year study, 43% of patients in the intervention groups and 66% of controls had developed type 2 diabetes. The corresponding figures at 20 years were found to be 80% and 93%, respectively.

The researchers found in multivariate analyses controlling for age and clustering by clinic that the people in the intervention groups had a 43% lower incidence of diabetes over the 20-year period (hazard ratio 0.57; 95% confidence interval 0.31-0.81).

There were no significant differences between the intervention and control groups in terms of risk of CVD events, or all-cause mortality. CVD mortality tended to be lower in the people who were in the intervention groups, but this was not significantly lower than the rate in the control group.

Guangwei Li, from the China-Japan Friendship Hospital in Beijing concluded: “Group-based lifestyle interventions provided over 6 years can prevent or delay type 2 diabetes for up to 14 years after the active intervention. Whether lifestyle intervention also leads to a reduction in CVD events and mortality remains unclear.”

Source: American Diabetes Association’s 68th Scientific Sessions, San Francisco, USA, 6-10 June 2008, presentation number 260 OR.

Continuous glucose monitoring data provide insight into insulin effects and risks

Continuous glucose monitoring (CGM) data from the 4-T trial have provided new insights into the effects of biphasic, prandial, and basal insulin use on glucose control and hypoglycaemia risks. Researchers from centres in Leicester and Oxford, UK, reported CGM results from the Treating to Target in Type 2 Diabetes (4-T) trial. The 4-T trial is a randomised multi-centre study in the UK and Ireland investigating the addition of biphasic insulin twice daily, prandial insulin aspart three times daily, or basal insulin detemir once or twice daily, in patients with type 2 diabetes and HbA1c 7-10% on the maximum tolerated dose of metformin.
and sulphonylurea therapy.

For the CGM part of the study, the researchers analysed data from 102 patients who were monitored for up to 72 hours, and who kept diary records of meals and hypoglycaemic events. Of the 102 patients, 33 were taking biphasic insulin, 31 were taking prandial insulin, and 38 were taking basal insulin.

The proportion of CGM values in target – defined as glucose levels of 4-5.5 mmol/l between meals and 4-7 mmol/l for 3 hours after each meal – was highest in the prandial insulin group (32.7%), and did not differ for the biphasic (24.6%) and basal (24.9%) insulin groups.

In the biphasic group, the mean numbers of biochemical hypoglycaemic events per patient per week were 5.5 (all hypoglycaemia), 6.3 (daytime hypoglycaemia), and 3.5 (night-time hypoglycaemia). In the prandial group the numbers were 3.4, 3.9, and 2.4, respectively, while in the basal group the numbers were 2.1, 2.3, and 1.1, respectively. The risk of hypoglycaemia was significantly lower in the basal group compared with the other two groups.

Concluding, the researchers said the findings are consistent with those from the main 4-T trial, showing that patients in the basal group spent less time within glycaemic targets, and had the lowest hypoglycaemic risk. In addition, the risk of hypoglycaemia did not differ in the biphasic and prandial groups.

Source: American Diabetes Association’s 68th Scientific Sessions, San Francisco, USA, 6-10 June 2008, presentation number 390 OR.

Pioglitazone for Prediabetes Greatly Reduces Disease Progression

People with impaired glucose tolerance (IGT) were 81% less likely to develop type 2 diabetes over a 3-year period if treated with pioglitazone, according to a prospective, randomised, double-blind, placebo-controlled study of 602 patients. One new case of diabetes could be avoided per year for every 3.5 patients treated with pioglitazone for IGT, Ralph DeFronzo said at the Annual Scientific Sessions of the ADA.

The 303 patients on the pioglitazone also significantly improved on measures of insulin resistance and beta-cell function, while there were no significant changes in the 299 patients on placebo. In the pioglitazone group, 1.5% of patients/year developed diabetes, compared with 6.8% per year on placebo. IGT reverted to normal glucose tolerance in 42% of the pioglitazone group by the end of the study, compared with 28% on placebo.

There are no medications approved for the treatment of prediabetes to prevent progression to diabetes. Metformin probably is the most common off-label treatment used for this purpose, in DeFronzo’s trial, called the Actos Now for Prevention of Diabetes (ACT NOW) study, patients started with an average BMI of 34 kg/m² and gained a mean of 3.5 kg in the pioglitazone group and 0.7 kg in the placebo group over a mean 2.6-year follow-up.

Patients had a mean age of 52 years and were recruited in eight medical centres over a 2-year period, then followed for at least 2 more years or until a diabetes diagnosis. All had 2-hour glucose values of 7.7-11.0 mmol/l on OGTT, a FPG concentration of 5.2-6.9 mmol/l, and one or more other high-risk characteristics: at least one component of the metabolic syndrome, a family history of type 2 diabetes, a history of gestational diabetes, the presence of polycystic ovary syndrome, or minority ethnicity.

A combination of IGT and IFG was present in 68% of patients, and the rest had isolated IGT. Compared with 102 healthy matched controls, patients in the study showed a 48% reduction in insulin sensitivity and a 78% decrease in the insulin secretion/insulin resistance index.

Patients were randomised to treatment with placebo or 30 mg/day pioglitazone. If the drug was tolerated after 1 month, the dose could be increased up to 45 mg/day. “What was quite surprising was how quickly pioglitazone dropped the fasting glucose,” DeFronzo said. “Within the first 3 months of initiating pioglitazone, there was a defined decrease in glucose” separating the two groups that was maintained to the end. The study had 90% power to detect at least a 50% reduction in progression to diabetes in the treatment group vs. placebo.

Future research should examine whether treating prediabetes with TZDs or metformin delays progression to diabetes or prevents it, and whether these drugs reduce cardiovascular risk. Approximately 21 million people in the United States have IGT, which puts them at risk for diabetes and for cardiovascular disease, DeFronzo said. From 3% to 13% of people with IGT go on to develop diabetes.
Physical Activity Key in Combating Childhood and Adolescent Obesity

Increasing physical activity levels in children and adolescents is just what the doctor should order to reverse the rate of childhood and adolescent obesity, Dénes Molnár, professor in the department of paediatrics at the University of Pécs (Hungary).

Molnár reviewed the current literature discussing the role of physical activity and obesity prevention and management. He said he found good evidence linking health advantages with increased physical activity. “There is an inverse relation between changes in physical activity levels and changes in [body mass index] and adiposity,” Molnár said at the 16th European Congress on Obesity. “Recent studies have shown positive association between vigorous physical activity and cardiovascular fitness and a negative association between vigorous physical activity and fatness.”

Recent data have shown that 15% of European children attending obesity centres suffer from metabolic syndrome. Physical inactivity adds to the complications of obesity, with statistics showing that 37% of coronary heart disease can be attributed to physical inactivity, compared with 19% and 13% from smoking and high blood pressure, respectively.

The study found that the percentage of American high school students participating in daily physical education classes is decreasing. In addition, studies show that the number of cars per family as well as the number of television sets per household has increased in a parallel fashion with obesity rates. Many studies indicate that the more time is spent watching television, the higher the rates of obesity.

A review of a cohort of studies in children has shown that high physical activity was associated with low obesity over time, and vice versa. The amount of physical activity steeply decreases as children get older, especially in girls.

He noted that inactive children in their childhood will likely continue to remain inactive during adulthood, which makes increasing the level of physical activity in children that much more important.

He discussed one study he did with an accelerometer as part of the HELENA (Healthy Lifestyle in Europe by Nutrition in Adolescence) study. He looked at 2,000 children, aged 13.0-16.9 years; half the subjects were male. Study subjects performed moderate physical exercise 60 minutes per day. Preliminary data showed that boys did much better than girls in terms of their level of physical activity; however, on average only 55% of all the children and only 25% of the girls were acceptably physically active.

Trials have shown that those individuals who take part in increased or vigorous activity demonstrate a much more pronounced weight loss. However, physical activity usually does not increase short-term diet-induced weight loss.

In addition, there are other parameters of increased physical activity – aside from weight reduction and body fat reduction – that improve health, such as improved levels of cholesterol and triglycerides. Individuals that participate in long-term exercise programmes demonstrate a significant increase in HDL cholesterol levels.

The listed health benefits of regular exercise include: lengthened lifespan; decreased morbidity and mortality from cardiovascular disease (a result of moderated blood pressure, decreased total cholesterol and LDL cholesterol, increased HDL cholesterol, and decreased triglycerides); improved bone density; improved cardio-respiratory response; and improved control of diabetes and glucose metabolism.

“A healthy approach in combating childhood obesity is multi-strategic and multidisciplinary, and includes an increase actual physical activity, increase school-based physical activity, decreased sedentary behaviour, and modified eating behaviour.”

It must be noted that family involvement is essential to the process.
Mohammed Abdul-Ghani, a researcher in the Diabetes Division of the University of Texas Health Science Center at San Antonio, USA, discussed at the 68th Scientific Sessions of the ADA, progress in differentiating impaired glucose intolerance (IGT) from impaired fasting glucose (IFG). The new data directly affect how these should be considered clinically.

He reported that these values, although commonly occurring in the same patient, measure two very different pathologic processes. In summary he stated:

- As pathologic indicators, IGF and IGT measure completely different processes and should not be considered interchangeable.
- Abnormal IFG levels are driven by decreased glucose clearance, increased insulin resistance in the liver, and are accompanied by relatively normal 2-hour plasma glucose levels after a meal.
- Abnormal IGT levels are driven by impaired insulin secretion in the beta-cell and are accompanied by high 2-hour plasma glucose levels after a meal.
- If treatment is being considered for these glucose abnormalities: increased physical activity will be more effective for IFG, while metformin will be more effective for IGT.
- The current findings have relevance to the debate about the use of the oral glucose tolerance test (OGTT) because of the inability of FBG alone to reflect IGT.

Source: 68th Scientific Sessions of the American Diabetes Society in San Francisco, USA.

Editors Note: The US Diabetes Prevention Program and other studies have demonstrated that lifestyle modification is superior to metformin in preventing or delaying the onset of T2DM in people with IGT

One in 3 diabetes patients with Atherosclerotic Vascular Disease not receiving statins and antiplatelet therapy

About one in every three patients with type 2 diabetes and known atherosclerotic vascular disease (AVD) is not receiving statins or antiplatelet therapy, according to a national survey conducted in Germany.

Researchers from the Center for Clinical Studies GWT in Dresden, Germany, analysed data provided by 238 GP and diabetologist practices, covering a total of 4,020 patients with type 2 diabetes (10-30 consecutive patients per practice) aged 35-80 years.

The overall prevalence of AVD (a history of myocardial infarction, stroke, or revascularization) in this population was 10.7%, of whom 66% were receiving statins and 72.9% were receiving antiplatelet therapy (in accordance with national guidelines which suggest the use of statins and antiplatelet agents in patients with type 2 diabetes and cardiovascular disease).

In the patients without AVD, the percentages receiving statins and antiplatelet therapy were 27.6% and 22.9% respectively.

The researchers subdivided the group of patients without AVD into three groups according to their risk of developing cardiovascular disease in the next 10 years, based on their Framingham score: 30.3% of patients had a low risk, 26% had a moderate risk, and 43.7% had a high risk. In the high-risk group, only 27.6% of patients were receiving lipid lowering agents and only 20.6% were receiving antiplatelet agents.

The researchers concluded that a history of AVD significantly increases the likelihood of receiving statins and antiplatelet therapy: “However, still one-third of patients with known AVD neither got statins nor antiplatelet treatment.”

Source: American Diabetes Association’s 68th Scientific Sessions, San Francisco, USA, 6-10 June 2008, presentation number 634P.