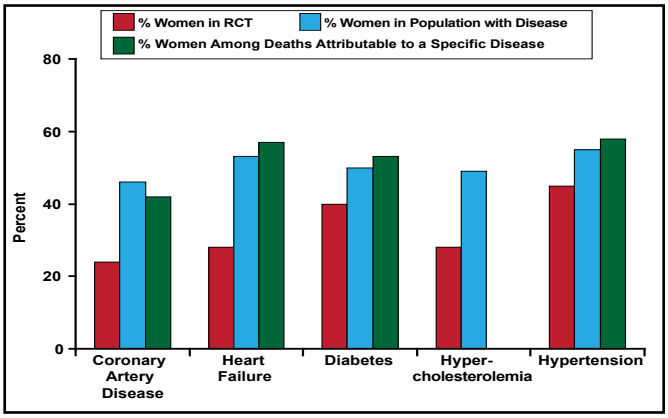
proven therapies in women, the enrollment of women in RCTs remains low, relative to their overall representation in disease populations (Figure 1) [Melloni C et al. *Circ Cardiovasc Qual Outcomes* 2010]. To ensure that the evidence that supports treatment is relevant to women, more attention must be focused on increasing recruitment of women into randomized clinical trials.

Figure 1. Inclusion of Women in RCTs Supporting Women's Prevention Guidelines.



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China Da Qing Study: Lifestyle Change in Women With IGT Extends Life

Written by Rita Buckley

Twenty-three years of follow-up data from the China Da Qing Diabetes Prevention Study (CDQPDS) show that lifestyle intervention to prevent diabetes can reduce all-cause and cardiovascular (CV) mortality among women with impaired glucose tolerance (IGT) but not among men. Findings from the study were reported by Guangwei Li, MD, Department of Endocrinology, China-Japan Friendship Hospital, Beijing, China.

In 1986, 577 adults with IGT from 33 clinics in Da Qing, China, were randomly assigned to a control group or 1 of 3 lifestyle intervention groups (diet, exercise, or diet plus exercise). Active intervention was carried out from 1986 to 1992. Participants who were assigned to the exercise group or diet-plus-exercise group were encouraged to increase the amount of their physical activity by at least 1 unit per day (as defined in Table 1) and by 2 units per day, if possible, for participants aged <50 years with no evidence of CV disease (Table 1) [Pan XR et al. *Diabetes Care* 1997].

A 20-year follow-up study showed that group-based combined lifestyle interventions over 6 years in people with IGT can prevent or delay diabetes for up to 14 years after the active intervention [Li G et al. *Lancet* 2008]. Lifestyle intervention for 6 years in IGT was also associated with a 47% decline in the incidence of severe, vision-threatening retinopathy over 20 years [Gong Q et al. *Diabetologia* 2011].

Table 1. Activities Required for Increasing Activity by One Unit of Exercise.

Intensity	Time (min)	Activity
Mild	30	Slow walking, shopping, house cleaning
Moderate	20	Faster walking, cycling, heavy laundry, ballroom dancing
Strenuous	10	Slow running, climbing stairs, volley ball, table tennis
Very strenuous	5	Jumping rope, basketball, swimming

The aim of the current trial was to examine all-cause and CV mortality among those who participated in the 6-year lifestyle intervention that was implemented in the Da Qing Diabetes Prevention Study. In 2009, 23 years after randomization, participants were traced to determine the long-term impact of the interventions on mortality; 47 women and 127 men had died.

Mortality rates were compared between the control groups and the combined intervention groups (diet, exercise, and diet plus exercise). All-cause mortality was defined as death from any cause. CV mortality was defined as death from coronary heart disease, stroke, and sudden death.

In women, combined lifestyle intervention (diet, exercise, and diet plus exercise) reduced all-cause mortality by 53% (hazard rate ratio [HRR], 0.47; 95% CI, 0.25 to 0.86), with cumulative all-cause mortality of 16.2% (95% CI, 11.2 to 21.2) in the intervention group versus 29.3% (95% CI, 17.5 to 48.0) in the control group (p=0.02). Among men, there was no significant difference in cumulative all-cause mortality (p=0.41) between the combined intervention and control groups (41.1% versus 46.7%).

The reduction in all-cause mortality in women was mainly because of differences in CV mortality (heart disease and stroke; HRR, 0.30; 95% CI, 0.12 to 0.68), with 23-year cumulative mortality of 6.8% in the intervention group (95% CI, 3.4 to 10.2) versus 18.8% (95% CI, 8.8 to 28.8) in the control group (p=0.006). In men, there was also no significant difference in cumulative CV mortality (p=0.47) in the combined intervention and control groups (26.4%; 95% CI, 21.1 to 31.6 versus 27.4; 95% CI, 18.6 to 32.2).

Data from the intervention groups (diet, exercise, and diet plus exercise) suggest that combined lifestyle intervention significantly lowers all-cause and CV mortality among

women with IGT but not among men. Reasons may include a large difference in baseline smoking rates between men and women.

Apart from diabetes, measures of risk factors for death (and CV disease) at baseline and during the trial were limited. In turn, the investigators were unable to identify or exclude possible confounding factors for the differences in outcomes between women and men. The reasons remain unclear.

Participants in the intervention group were, on average, 2 years younger than those in the control group, but there were no differences in baseline body mass index (BMI) in controls, 26.2±0.2 kg/m^2 versus BMI in the combined intervention group, 25.7±0.2 kg/m^2. The changes in body weight during the active-intervention period (1986 to 1992) and the entire follow-up period (1986 to 2006) did not differ significantly by group [Guangwei L et al. *Lancet* 2008].

Markers of Macrovascular Complications in Pediatric Diabetes

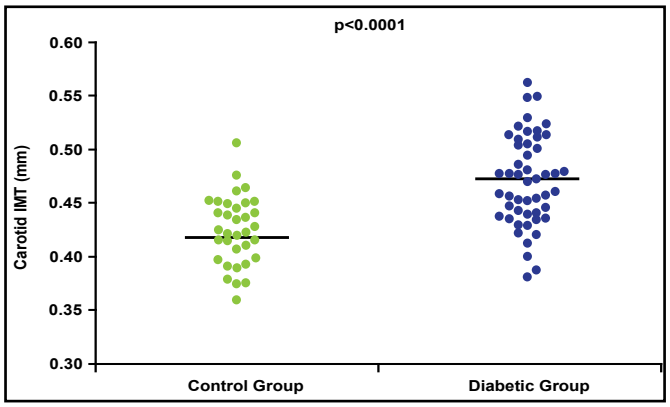
Written by Phil Vinall

Children with diabetes are at high risk for premature cardiovascular disease (CVD), which can lead to mortality later in life. Screening and treatment of modifiable risk factors in young patients with diabetes are important to decrease lifetime risk for CVD. R. Paul Wadwa, MD, University of Colorado School of Medicine, Aurora, Colorado, USA, discussed several noninvasive surrogate measures that would allow for the stratification of CVD risk, and he presented evidence for more aggressive treatment of patients at the highest risk for macrovascular disease in adulthood.

Endothelial dysfunction is considered an early stage in the pathogenesis of atherosclerosis. Evidence indicates that endothelial dysfunction in children with diabetes may predispose them to the development of early atherosclerosis [Järvisalo MJ et al. *Circulation* 2004]. The brachial ultrasound technique can be beneficial for detecting impaired flow-mediated dilation. Another tool for measuring endothelial dysfunction is peripheral arterial tonometry. In one study, children with type 1 diabetes had endothelial dysfunction, as evidenced by lower mean reactive hyperemia peripheral artery tonometry scores when compared with children without diabetes [Haller M et al. *Pediatr Diabetes* 2007].

Noninvasive B-mode ultrasonographic measurement of progression of intima-media thickness in the distal common carotid artery is a useful surrogate endpoint for clinical coronary events. Increases in the thickness of the intima and media of the carotid artery are directly associated with an increased risk of myocardial infarction and stroke in older adults without a history of CVD [O'Leary DH et al. *N Engl J Med* 1999]. Although data are limited in younger patients, one study has shown an increase in carotid intima-media thickness (cIMT) and a decrease in flow-mediated dilation in children (mean age 11 years) with type 1 diabetes (Figure 1) [Järvisalo MJ et al. *Circulation* 2004]. Preliminary data presented at the 2011 meeting of the American Diabetes Association indicate significantly thicker cIMT in the common and internal carotid in youth with type 1 diabetes compared with controls [Urbina EM et al. *Diabetes* 2011].

Figure 1. cIMT in Controls and Type 1 Diabetes.



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In an ancillary study to the SEARCH for Diabetes in Youth study, the measurement of arterial stiffness by pulse-wave velocity, pulse-wave analysis, and brachial artery distensibility indicated that youths with type 2 diabetes had worse arterial stiffness than youths with type 1 diabetes [Wadwa RP et al. *Diabetes Care* 2010]. Further, pulse-wave velocity was higher than controls in youths with type 1 diabetes with a mean age of 19 years but not in youths with a mean age of 15 years, suggesting that the right time for aggressive intervention to prevent vascular damage would be between the ages of 15 to 19 years [Wadwa RP et al. *Diabetes* 2011 (two ADA abstracts)].

Coronary artery calcification correlates with overall coronary plaque burden and can be predictive of future coronary events. Although data in adults with diabetes are strong, coronary artery calcification may be of lesser interest in pediatric patients, as there is a relatively low presence of coronary artery calcification in patients aged <30 years [Starkman HS. *Diabetes Care* 2003].

Echocardiography has been used to document cardiac dysfunction in adults with diabetes. Recent studies have shown that it can detect diastolic dysfunction, increased ventricular septal thickness, and lower circumferential strain compared with nondiabetic controls [Nadeau K