The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study

Guangwei Li, Ping Zhang, Jinping Wang, Edward W Gregg, Wenying Yang, Qiuhong Gong, Hui Li, Hongliang Li, Yayun Jiang, Yali An, Ying Shuai, Bo Zhang, Jingling Zhang, Theodore J Thompson, Robert B Gerzoff, Gojka Roglic, Yinghua Hu, Peter H Bennett

Summary

Background **Intensive lifestyle interventions can reduce the incidence of type 2 diabetes in people with impaired glucose tolerance, but how long these benefits extend beyond the period of active intervention, and whether such interventions reduce the risk of cardiovascular disease (CVD) and mortality, is unclear. We aimed to assess whether intensive lifestyle interventions have a long-term effect on the risk of diabetes, diabetes-related macrovascular and microvascular complications, and mortality.**

Methods **In 1986, 577 adults with impaired glucose tolerance from 33 clinics in China were randomly assigned to either the control group or to one of three lifestyle intervention groups (diet, exercise, or diet plus exercise). Active intervention took place over 6 years until 1992. In 2006, study participants were followed-up to assess the long-term effect of the interventions. The primary outcomes were diabetes incidence, CVD incidence and mortality, and all-cause mortality.**

Findings **Compared with control participants, those in the combined lifestyle intervention groups had a 51% lower incidence of diabetes (hazard rate ratio [HRR] 0·49; 95% CI 0·33–0·73) during the active intervention period and a 43% lower incidence (0·57; 0·41–0·81) over the 20 year period, controlled for age and clustering by clinic. The average annual incidence of diabetes was 7% for intervention participants versus 11% in control participants, with 20-year cumulative incidence of 80% in the intervention groups and 93% in the control group. Participants in the intervention group spent an average of 3·6 fewer years with diabetes than those in the control group. There was no significant difference between the intervention and control groups in the rate of first CVD events (HRR 0·98; 95% CI 0·71–1·37), CVD mortality (0·83; 0·48–1·40), and all-cause mortality (0·96; 0·65–1·41), but our study had limited statistical power to detect differences for these outcomes.**

Interpretation **Group-based lifestyle interventions over 6 years can prevent or delay diabetes for up to 14 years after the active intervention. However, whether lifestyle intervention also leads to reduced CVD and mortality remains unclear.**

Funding **Centers for Disease Control and Prevention, WHO, the China-Japan Friendship Hospital, and Da Qing First Hospital.**

Lancet 2008; 371: 1783–89

See **Comment** page 1731

Department of Endocrinology, China-Japan Friendship Hospital, Beijing, China (Prof G Li MD, Prof W Yang MD, Q Gong MD, Ho Li PhD, Y An MD, Y Shuai MS, B Zhang MD); **Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA** (P Zhang PhD, E W Gregg PhD, T J Thompson MS, R B Gerzoff MS); **Department of Cardiology, Da Qing First Hospital, Da Qing, China** (J Wang MD, Hu Li MD, Y Jiang BS, J Zhang RS, Y Hu MD); **Department of Chronic Diseases and Health Promotion, World Health Organization, Geneva, Switzerland** (G Roglic MD); **and Phoenix Epidemiology and Clinical Research Branch, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Phoenix, AZ, USA** (P H Bennett FRCP)

Correspondence to:
Dr Ping Zhang
Division of Diabetes Translation, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta 30341, GA, USA
pzhang@cdc.gov

or

Prof Guangwei Li
Department of Endocrinology, China-Japan Friendship Hospital, Beijing 100029, China
guangwei_li@medmail.com.cn

Introduction

Major clinical trials in the USA, China, India, Finland, and Japan[1–5] have shown the effectiveness of lifestyle interventions to reduce the incidence of diabetes in people with impaired glucose tolerance. Interventions designed to achieve modest weight loss and enhance behavioural change were effective across sex, age, and race or ethnicity groups, and over different bodyweights. The interventions used group or individual counselling to reduce total dietary intake and saturated fat, increase dietary fibre, exercise, and self-monitoring of behaviours.

Despite these studies' importance as catalysts for new public health efforts, important questions remain. How long does the reduction in the incidence of diabetes persist? The Finnish Diabetes Prevention Study[6] is known to have assessed this question, reporting that diabetes incidence was reduced for 3 years after the 4-year active intervention. Also unclear is how much the benefits of diabetes prevention extend to reducing the complications of diabetes, such as myocardial infarction, stroke, and mortality.

The China Da Qing Diabetes Prevention Study[2] (CDQDPS) was the first of these large-scale trials and examined the effect of different lifestyle interventions in a group setting among Chinese people with impaired glucose tolerance. We report the results from a 20-year follow-up of the CDQDPS, in which 98% (568 of 577) of the participants were reassessed to establish the effect of lifestyle interventions on diabetes and other related health outcomes in people at high risk for diabetes.

Methods

Details of the design, methods, and population of the CDQDPS have been published previously.[2] Briefly, the CDQDPS investigated the effect of dietary and exercise intervention, alone and in combination, on incidence of

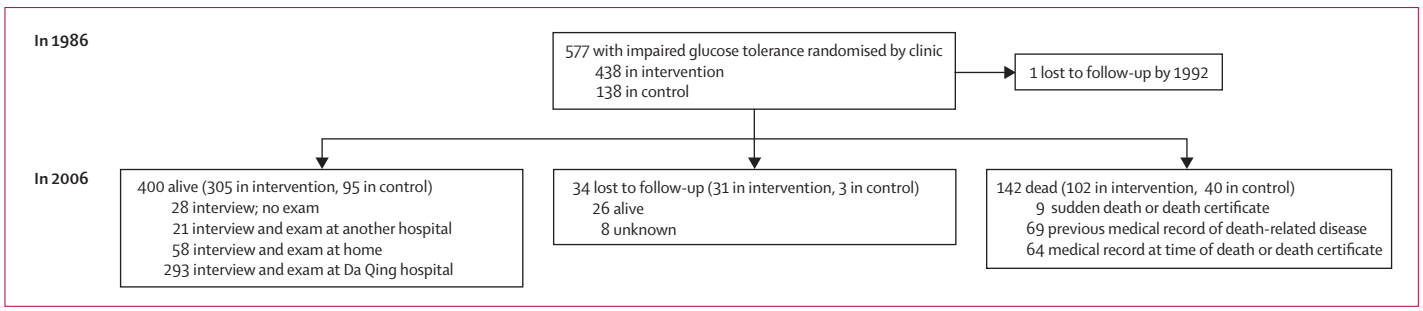

Figure 1: **Trial profile**

type 2 diabetes in people with impaired glucose tolerance. In 1986, 577 adults with impaired glucose tolerance at 33 clinics in Da Qing city, China, were recruited and randomised by clinic into either a control group or one of three lifestyle interventions: diet, exercise, or diet plus exercise. The goal of the diet intervention was to increase participants' vegetable intake and lower their alcohol and sugar intake. Those who were overweight or obese were also encouraged to lose weight by reducing their total calorie intake. The goal of the exercise intervention was to increase leisure time physical activity. The effect of the intervention was assessed at 2-yearly intervals. In 1992, after a 6-year intervention, participants were informed of the final results and asked to continue with normal medical care.

Our trial, the China Da Qing Diabetes Prevention Outcomes Study (CDQDPOS), was a longitudinal follow-up of CDQDPS participants over 20 years. The main objectives were to examine the intervention's long-term effect on the risk of diabetes, diabetes-related macrovascular and microvascular complications, and mortality. The primary outcomes were diabetes incidence, cardiovascular disease (CVD) incidence and mortality, all-cause morality, and any diabetes related microvascular and macrovascular complications. The secondary outcomes were specific microvascular and macrovascular diseases, risk factors for cardiovascular disease, health-related quality of life, and use of health care. The institutional review boards at WHO and the China-Japan Friendship Hospital approved the protocol. All study participants or relatives who provided information about deceased participants gave written informed consent.

Diabetes status was defined by self-reported diagnosed diabetes plus evidence of raised glucose levels in the medical record, taking hypoglycaemic medications, or fasting glucose and oral glucose tolerance tests, done every 2 years during the active intervention period (1986–1992) and at the end of follow-up (2006), and interpreted using 1985 WHO criteria for diabetes.[7] CVD events were defined as the first nonfatal or fatal cardiovascular events including myocardial infarction, sudden death, stroke, or amputation. Besides clinically diagnosed myocardial infarction, we also defined myocardial infarction cases on the basis of ECG results obtained during the physical examination with Minnesota codes 1·1 or 1·2+(5·1 or 5·2) or 1·3+(5·1 or 5·2).

Mortality outcomes included CVD death and all-cause death. Because death certificates in China are not routinely retained beyond 10 years, information from multiple sources was used to determine cause of death, including available death certificates, history of disease, major symptoms as reported by the relative, and the cause of death assigned by the responsible physician from hospital records. From a review of this information, two physicians, blinded to the participant's intervention, independently determined and assigned the underlying cause of death. A third physician (also blinded to the intervention) settled any disagreements. Only a general classification of cause of death was used (stroke, heart disease or any other CVD, cancer, injuries, diabetes or renal, and other).

Follow-up data for living participants in the Da Qing area were collected by personal interview, clinical examination, including a 75-g oral glucose tolerance tests and 12-lead electrocardiogram, and medical record review to determine diabetes and cardiovascular disease status and date of diagnosis of diabetes or cardiovascular events. For those outside the Da Qing area, the interview was done by phone and their local health provider did the clinical examination. For deceased participants, data were obtained by proxy interview from a living relative (spouse, sibling, or child) and medical record review. Trained abstracters, masked to the participant's intervention status, reviewed the medical records.

Our primary analysis compared diabetes incidence, CVD incidence, CVD mortality, and all-cause mortality between the control group and the combined intervention group. We combined these groups a priori because they did not differ significantly in diabetes incidence during the active-intervention period and due to concerns about statistical power. Incidence for each outcome was calculated as the number of events divided by total person-years of exposure, with censoring at the time of the diagnosis, death, loss to follow-up, or Dec 31, 2006. Hazard rate ratios (HRRs), adjusted for age and for clustering by clinic, were determined using a Weibol proportional hazards survival model. Age, defined as a continuous variable, was included in the models as a fixed effect and clinic as a random effect.

We also assessed HRRs for CVD incidence, CVD mortality, and all-cause mortality in the post-intervention period (1993–2006). We estimated the relative risk to see whether the intervention effect varied during follow-up. We recalculated person-years of exposure from the end of the intervention (1992) through the end of follow-up (2006) by excluding the cases accrued during the intervention period (1986–1992). Diabetes was not included in the post-intervention analyses since 265 patients had already developed diabetes by the end of the active intervention period, thus greatly truncating and biasing the available sample entering the post-intervention period. The above analyses were based on intention to treat and were done with the NLMIXED procedure in SAS version 9.1.2 (SAS Institute, Cary, NC, USA).

We also used multilevel discrete time survival models to estimate a time-varying HRR between treated and control groups,[8] which allowed us to estimate whether the intervention effect deteriorated over time.[9] The HRR was treated as a random effect and separate ratios for each follow-up year were estimated. Clinic was included in these models as a random effect, but age was not, since its inclusion results in data too sparse for fitting these models. Because of the randomised design, these comparisons are valid without adjusting for covariates. These time-varying HRR models were fit using WinBUGS.[10]

Role of the funding source

Centers for Disease Control and Prevention, WHO, the China-Japan Friendship Hospital, and Da Qing First Hospital were co-sponsors of this follow-up study. Scientists from these organisations were involved in the study design, collection, analysis, interpretation of the data, and the writing of the report. The authors had full access to all data in the study and had the final responsibility to submit for publication.

Results

Of the original 577 CDQDPS participants, one could not be traced at the end of the active intervention in 1992. By 2006, 142 (25%) had died and 426 (74%) were alive on Dec 31, 2006 (figure 1). Eight could not be traced and were lost to follow-up. For 26, only data from the active intervention period or from medical records during the post-intervention period were obtained. For the remainder (400), 293 were interviewed and examined at the Da Qing First Hospital and 79 were interviewed at home, of whom 58 were examined. For those living outside the Da Qing area (28), the interview was done by phone, and 21 of these participants were examined by their health providers. Of the 426 living participants, 372 (87%) had the interview and had a clinical examination. The medical records of 396 alive and 64 deceased participants were obtained. At the end of follow-up, 153 people were eligible for oral glucose tolerance tests, but only 128 received the test and 25 had a fasting plasma glucose test at their homes. Of the 577 CDQDPS participants, valid follow-up information was obtained for 98% (563) for diabetes, 94% (542) for any CVD events, and 98% (568) for CVD and all-cause mortality. The total number of person-years of follow-up was 5268 for the diabetes outcome (range 1–20, median 6, IQR 11, mean 9·4 years), 8817 for the CVD-event outcome (range 1–20, median 20, IQR 7, mean 16·3 years), and 9699 for the CVD and all-cause mortality outcome (range 0·2–20, median 20, IQR 2, mean 17·9 years). No adverse events were recorded.

Participants in the intervention group were on average 2 years younger than in the control group, but there were no differences in baseline body-mass index, lipid, or fasting glucose levels (table 1). Differences in blood pressure and total cholesterol concentrations between the two groups were not significant by 1992, the end of

	Control	Combined intervention
1986		
Total	(n=138)	(n=438)
Age (years)	46·6 (0·8)	44·7 (0·4)
Sex (men/women)	79/59	233/205
Body-mass index (kg/m²)	26·2 (0·3)	25·7 (0·2)
Blood pressure (mm Hg)		
Systolic	134·3 (2·0)	132·2 (1·1)
Diastolic	88·5 (1·5)	87·2 (0·7)
Total cholesterol (mmol/L)	5·26 (1·02)	5·21 (1·01)
Fasting glucose (mmol/L)	5·52 (0·07)	5·60 (0·04)
2-h glucose level (mmol/L)	9·02 (0·08)	8·97 (0·02)
1992		
Total	(n=133)	(n=397)
Body-mass index (kg/m²)	25·8 (0·33)	25·2 (0·18)
Blood pressure (mm Hg)		
Systolic	132·1 (1·8)	130·8 (1·1)
Diastolic	85·0 (1·1)	85·0 (0·7)
Total cholesterol (mmol/L)	5·31 (1·02)	5·26 (1·01)
Fasting glucose (mmol/L)	7·58 (0·23)	7·0 (0·17)
2-h glucose level (mmol/L)	12·5 (0·48)	10·63 (0·22)*
Change in body-mass index from 1986 to 1992 (kg/m²)	−0·34 (0·19)	−0·69 (0·10)
Change in weight from 1986 to 1992 (kg)	−0·89 (0·52)	−1·88 (0·28)
2006		
Body-mass index (kg/m²)	(n=82) 24·4 (0·29)	(n=266) 24·5 (0·9)
Blood pressure (mm Hg)	(n=87)	(n=285)
Systolic	145·0 (2·1)	144·6 (1·2)
Diastolic	82·8 (1·3)	82·4 (0·7)
Total cholesterol (mmol/L)	(n=83) 5·21 (1·02)	(n=262) 5·10 (1·01)
Fasting glucose (mmol/L)	(n=80) 8·7 (0·35)	(n=260) 7·9 (0·2)†
2-h glucose level (mmol/L)	(n=28) 13·8 (1·1)	(n=100) 11·5 (0·50)†
Change in body-mass index from 1986 to 2006 (kg/m²)	(n=82) −1·57 (0·29)	(n=266) −1·41 (0·18)
Change in weight from 1986 to 2006 (kg)	(n=82) −4·2 (0·8)	(n=266) −3·7 (0·5)

Data are mean (SE). *p<0·0001. †p<0·05.

Table 1: **Characteristics of study participants by group at baseline (1986), end of the 6-year active intervention (1992), and end of follow-up (2006)**

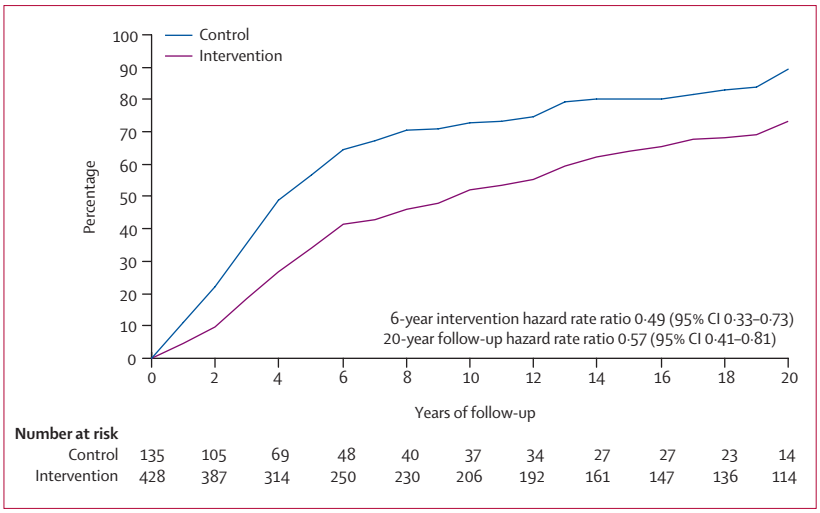

Figure 2: **Cumulative incidence of diabetes mellitus during follow-up in China Da Qing Diabetes Prevention Outcome Study**

	Incidence per 100 person years per year (95% CI)		Cumulative incidence, % (95% CI)		Multivariate adjusted HRR* (95% CI)
	Control	Intervention	Control	Intervention	
Active intervention					
Diabetes					
1986–1992	14·1 (11·2–17·0)	7·9 (6·8–9·1)	65·8 (57·7–73·9)	42·8 (38·0–47·5)	0·49 (0·33–0·73)
1986–2006	11·3 (9·3–13·3)	6·9 (5·8–7·2)	92·8 (88·3–97·3)	79·7 (75·6–83·8)	0·57 (0·41–0·81)
Any first CVD events					
1986–1992	0·9 (0·2–1·6)	0·9 (0·5–1·3)	5·4 (1·5–9·2)	5·2 (3·0–7·3)	0·96 (0·76–1·44)
1986–2006	2·5 (1·9–3·2)	2·3 (1·9–2·7)	44·1 (35·3–53·0)	40·9 (36·0–45·9)	0·98 (0·71–1·37)
CVD mortality					
1986–1992	0	0·2 (0·0–0·3)	0	1·0 (0–1·9)	-
1986–2006	0·9 (0·5–1·3)	0·6 (0·5–0·8)	17·4 (10·6–24·2)	12·5 (9·1–15·8)	0·83 (0·48–1·40)
All-cause mortality					
1986–1992	0·6 (0·1–1·2)	0·7 (0·8–1·1)	3·7 (0·5–6·8)	4·3 (2·3–6·2)	1·33 (0·45–3·92)
1986–2006	1·7 (1·1–2·2)	1·4 (1·1–1·6)	29·3 (21·5–37·0)	25·0 (20·8–29·2)	0·96 (0·65–1·41)
Post-intervention					
Any first CVD events					
1993–2006	3·2(2·35–4·05)	2·9 (2·4–3·4)	41·9 (33·0–50·9)	38·5 (33·5–43·5)	0·98 (0·68–1·43)
CVD mortality					
1993–2006	0·9 (0·5–1·3)	0·6 (0·4–0·8)	17·4 (10·6–24·2)	11·6 (8·3–14·9)	0·73 (0·42–1·26)
All-cause mortality					
1993–2006	1·5 (1·0–2·0)	1·2 (0·9–1·4)	26·6 (18·9–34·2)	21·7 (17·6–25·8)	0·90 (0·59–1·37)

HRR=hazard rate ratio. CVD=cardiovascular disease. *Adjusted for age and clustering by clinic.

Table 2: **Incidence of diabetes, CVD, and mortality in the active intervention (1986–92) and entire follow-up period (1986–2006), and CVD and mortality in the post intervention period (1993–2006)**

the active intervention, or by 2006 in the survivors at the end of follow-up. The changes in bodyweight during the active intervention period (1986–1992) and the entire follow-up period (1986–2006) did not differ significantly by group.

Of the 577 participants in 1986, 435 had developed diabetes by the end of follow-up. 265 cases were identified by oral glucose tolerance tests during the active intervention phase, 145 were identified by report from the patient or relative, with additional evidence of either use of hypoglycaemic medication or raised glucose level recorded in the medical record at time of diagnosis during the post-intervention period. Finally, 25 cases were identified by oral glucose tolerance tests at the end of the study. The diabetes status of 14 participants was unknown.

During the active intervention, the cumulative diabetes incidence was 43% in the intervention group and 66% in the control group, and the number needed to treat to prevent a case of diabetes was five people (table 2). During the 20 year follow-up, the cumulative diabetes incidence was 80% in the intervention group and 93% in the control group, and the number needed to treat to prevent a case of diabetes was six people. Participants in the intervention group had an average of 3·6 fewer years with diabetes. In people with diabetes, comparing the active intervention group to the controls at the end of follow-up, fewer were on insulin (26% [82 of 314] *vs* 34% [41 of 121]) and they had lower average haemoglobin A_{1c} levels (7·34% *vs* 7·76%), but these differences were not significant (p=0·11 and p=0·07, respectively).

In multivariate analyses that controlled for age and clustering by clinic, participants in the combined intervention group had a 43% lower incidence of diabetes than those in the control group (HRR 0·57; 95% CI 0·41–0·81; table 2). Over 20 years, the yearly estimated HRRs ranged from 0·51 to 0·64, with intervention participants having a lower diabetes incidence throughout the study (data not shown). In a subanalysis of the effects of diet, exercise, and diet plus exercise versus control, the randomisation groups for the original study, the 20-year HRRs for diabetes were 0·58 (0·38–0·89), 0·51 (0·31–0·83), and 0·66 (0·41–1·09), respectively.

The cumulative incidence of all-cause mortality, first CVD events, and CVD mortality are presented in figure 3. During the 20-year follow-up, there were 211 first CVD events (145 strokes and 66 myocardial infarctions). There were a total of 142 deaths, of which 68 were attributed to CVD. No first CVD events were diagnosed by ECG only, since all had been previously diagnosed clinically. The cumulative incidence of first CVD event was 41% for intervention participants and 44% for controls (table 2). The cumulative CVD mortality rate was 28% lower in the intervention group (12%) than the control group (17%), but this difference was not significant, nor were differences in all-cause mortality (25% *vs* 29%). The estimated annual HRRs from the analysis of time-varying hazard rates ranged from 0·58 to 1·20 for first CVD event, 0·61 to 0·89 for CVD-mortality, and 0·67 to 0·95 for all-cause mortality.

In the post-intervention period, the intervention group had a 8% lower incidence of first CVD events (39% *vs* 42%), 33% lower CVD mortality (12% *vs* 17%), and 18% lower all-cause mortality (22% *vs* 27%) than the control group,

but these differences were not significant (table 2). The estimated HRRs from the analysis of time-varying hazard rates (data not shown) ranged from 0·58 to 1·27 for first CVD event, 0·61 to 0·89 for CVD mortality, and 0·67 to 0·95 for all-cause mortality.

Discussion

Our findings from the CDQDPOS indicate that the reduction in diabetes incidence seen during the 6-year period of active intervention persisted for two decades. Chinese participants with impaired glucose tolerance randomised to lifestyle intervention groups had a 43% lower diabetes incidence (age and clinic adjusted) for up to 14 years after the active intervention ceased, and diabetes onset was delayed an average of 3·6 years. These findings are consistent with those of the Finnish Diabetes Prevention Study,[6] where the relative risk reduction in diabetes incidence varied only slightly between the active intervention period and up to 3·5 years after the intervention. The CDQDPOS also showed that the risk of eventually developing diabetes in people with impaired glucose tolerance in the absence of intervention remains high for many years, since 93% of the controls developed diabetes over 20 years. Previous reports with shorter follow-up have suggested that 5–10% of those with impaired glucose tolerance develop diabetes every year, but that many revert spontaneously to normal glucose tolerance.[11,12]

Interpretation of the findings related to the intervention and CVD events and mortality is more complicated. The incidence of first CVD events and all cause mortality did not differ significantly between the combined intervention group and the control group. The overall adjusted HRR of death from CVD, however, was 17% lower in the intervention group, but 95% CIs were wide and the difference was not significant. The observation that each of the outcomes (all-cause mortality, CVD mortality, CVD incidence) seem to have a reduced incidence for people who had received the intervention is encouraging. Nevertheless, our findings leave the relation between lifestyle-based diabetes prevention and effect on CVD and mortality unresolved. Of the deaths due to CVD, 65% (44 of 68) were attributed to stroke and 35% to heart disease a pattern consistent with other reports from China where deaths attributable to cerebrovascular disease are particularly high.[13,14]

Since the original CDQDPS was not designed to examine the effects of intervention on vascular complications and mortality, the statistical power to detect reductions in incidence of CVD and mortality risk was restricted. Only a few studies have examined the effect of interventions for diabetes prevention on CVD. In people with impaired glucose tolerance, only the STOP-NIDDM study[15,16] using acarbose, and the 12-year follow-up of the Malmö study[17] using diet and tolbutamide, suggest that the incidence of CVD could be reduced with interventions that decrease the incidence of diabetes. Other long-term follow-up trials might provide conclusive answers to this question.[6,18]

The extended reductions in diabetes incidence seen in intervention participants in our study could be explained by three broad mechanisms. First, lifestyle interventions could have led to changes in usual behaviour that were maintained beyond the period of the study intervention. Second, the interventions might have led to changes in the preventive care and health promotion efforts provided

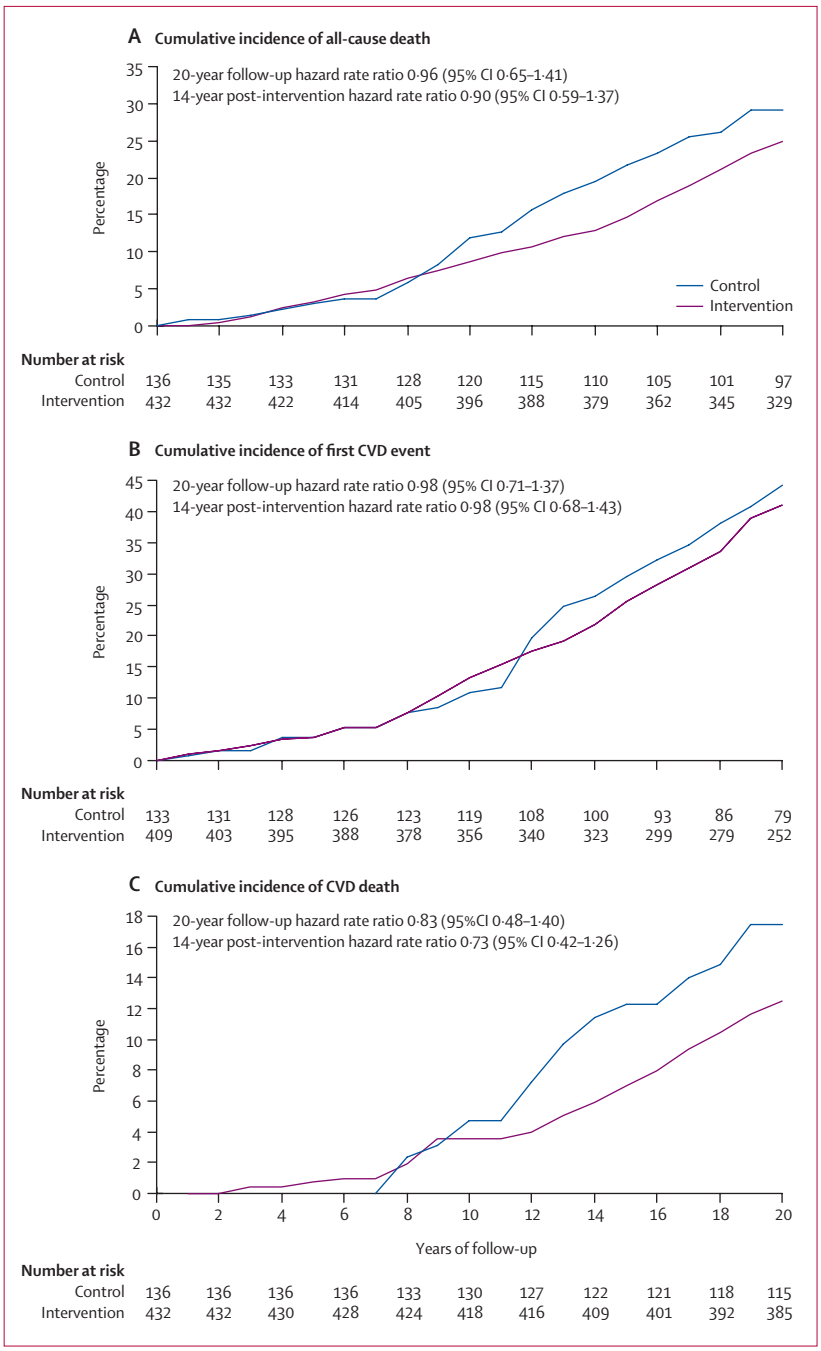

Figure 3: **Cumulative incidence of all-cause mortality (A), first CVD event (B), and CVD mortality (C) during follow-up in China Da Qing Diabetes Prevention Outcome Study**

by community clinics that had effects beyond the intervention period. Finally, lifestyle intervention might lead to some type of metabolic memory. Effects on insulin secretion or sensitivity that are well documented over the short term[19] might be maintained well beyond the active intervention in a manner analogous to the persistent changes that follow intensive insulin treatment for people with type 1 diabetes.[20]

Follow-up analyses of the Finnish Diabetes Prevention Study and the US Diabetes Prevention Program each suggested that weight-change was the mechanism for explaining reduced diabetes incidence.[4,6,21] However, we found little difference in weight-change between the intervention and control conditions during the active intervention, and we note that weight-change was also small in other successful prevention trials in other Asian populations.[3,5] Further analyses will be needed to establish whether exercise and diet reduce the incidence of type 2 diabetes independently of weight-change or by changing body composition, which might not be indicated by changes in bodyweight.

The CDQDPS was designed to investigate whether lifestyle interventions delivered to groups, rather than to individuals, could reduce the incidence of diabetes. The study, therefore, adopted a randomised cluster design, randomising participants on the basis of the clinics where they received their usual medical care. This design not only allowed for group instruction, but limited the possibility that participants in the active intervention groups could influence the behaviour of those in the control groups. This study used intervention techniques that needed few resources and could be applied to large populations. For analysis of the long-term effects of the interventions we decided a priori to pool groups of patients who had received diet, exercise, and diet plus exercise, because each of these interventions reduced diabetes incidence to a similar extent during the 6-year active intervention. Detailed subanalysis of the 20-year follow-up indicates that three intervention groups enjoyed similar long-term benefits, providing an additional post hoc justification for pooling these groups.

The high rates of ascertainment of the vital status of participants 14 years after the end of the active intervention, and inclusion of 94% of participants still living 20 years after randomisation, reduced any selective biases that might be attributable to loss to follow-up. Furthermore the follow-up interviews, examinations, and endpoint assessments were done by staff members who were unaware of the groups to which the participants were originally assigned, thus keeping interview or examiner bias to a minimum.

The main limitation of the CDQDPOS is that, beyond the 6-year active interventions, the participants were not re-tested periodically using standardised procedures. This passive ascertainment explains at least in part why we observed a lower diabetes incidence in the post-intervention period. The lower incidence rate of diabetes in the follow-up period than during the active intervention could also be because the people at highest risk had already converted or died sooner, leaving a lower risk pool of participants to convert at a slower rate during the extended follow-up. However, because the same ascertainment approach was used in the intervention and control groups, with an oral glucose tolerance test at the end of the study, passive ascertainment is unlikely to have led to a bias in our findings. Underlying causes of death were ascertained largely from proxy interviews supplemented by review of medical records, but the reports of causes of death within our broad categories seem unlikely to be biased by treatment group. There were no significant differences in the response rates to the questionnaire, medical record review, and physical examination by treatment assignments, and the percentage with events confirmed by medical record did not differ by vital status.

The lack of systematic clinical measurements during follow-up limited our ability to examine the effect of different risk factor changes and medical interventions on the study outcomes. Although data for some risk factors were obtained for survivors at the final visit, this information was potentially affected by survival bias and effects of treatment for comorbid conditions. Detailed information related to lifestyle changes was not obtained beyond the period of active intervention. Thus, we do not have data for weight and behaviour changes during follow-up, preventing conclusions about the contributions of changes in physical activity, weight, diet, or medications on outcomes. In 2006, surviving participants in the intervention and control groups reported no differences in total calorie intake from the main food items or amount of leisure time physical activity in the past year (data not shown). Although we achieved a 43% reduction in diabetes incidence in the intervention group, 80% of them still developed diabetes, albeit some 3·6 years later than the control group. Had the active period of intervention been for longer, then perhaps diabetes would have been averted in more of the participants.

The CDQDPOS has shown that, in Chinese people with impaired glucose tolerance, group-based interventions targeting lifestyle changes such as diet and exercise produce a durable and long-lasting reduction in incidence of type 2 diabetes. Our findings and the results from the 3-year follow-up of the Finnish Diabetes Prevention Study[6] suggest that the durable effects of lifestyle interventions extend across cultures. There were 33·2 million people with impaired glucose tolerance in China in 2003 and this amount is expected to increase to 54·3 million by 2025.[22] Small group and lifestyle counselling in high-risk individuals at community facilities is likely to be effective if aimed more broadly at the Chinese population, and might also be necessary in light of obesity trends in China.[23] At a more global level, widespread adoption of such interventions offers the prospect that projected increases in type 2 diabetes could

be attenuated. Since around 3 million excess deaths a year are attributable to diabetes worldwide,[24] lifestyle interventions seem to be a justifiable public health action both in developed and developing nations.

Contributors

GL and PZ coordinated the study and contributed to acquisition of funding, study design, statistical analysis, and draft and revision of the paper. JW and QG contributed to study design, acquisition of data, and statistical analysis. EWG contributed to study design, acquisition of funding, statistical analysis, and draft and revision of the paper. WY contributed to study design. GL, HuL, HoL, YJ YS, BZ, and JZ contributed to acquisition of data. YA contributed to acquisition of data and statistical analysis. TJT contributed to statistical analysis and draft of the paper. RBG contributed to statistical analysis and revision of the paper. GR contributed to study design, acquisition of funding, and revision of the paper. YH contributed to study design and acquisition of data. PHB contributed to study design, statistical analysis, and draft and revision of the paper.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

We thank the study participants in the original China Da Qing Diabetes Prevention Study and the China Da Qing Diabetes Prevention Outcome Study. This study was partially funded by CDC/WHO Cooperative Agreement number U58/CCU424123-01-02. We also thank Lingzhi Kong, China Ministry of Health, and the leadership at the China-Japan Friendship Hospital, Da Qing First Hospital, the Da Qing City Health Bureau, West Pacific Regional Office of WHO, and the WHO Beijing Office for their general support. We also thank Michael M Engelgau for his contribution to study design and David F Williamson for his constructive comments on the earlier version of the paper. Our special thanks go to the late Professor Pan Xiao Ren who originated the China Da Qing Diabetes Prevention Study, as without his leadership this study would not have been possible. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

References

1 Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; **346:** 393–403.

2 Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997; **20:** 537–44.

3 Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V. The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006; **49:** 289–97.

4 Tuomilehto J, Lindstrom J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; **344:** 1343–50.

5 Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract* 2005; **67:** 152–62.

6 Lindstrom J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet* 2006; **368:** 1673–79.

7 WHO. Diabetes mellitus: report of a WHO study group. Technical report series 727. Geneva: World Health Organization, 1985.

8 Efron B. Logistic regression, survival analysis, and the Kaplan-Meier curve. *J Am Stat Assoc* 1988; **83:** 414–25.

9 Gelman A HJ. Data analysis using regression and multilevel/hierarchical models. New York: Cambridge University Press, 2007.

10 Lunn DJ, Thomas A, Best N, Spiegelhalter D. WinBUGS—a Bayesian modelling framework: concepts, structure, and extensibility. *Stat Comput* 2000; **10:** 325–37.

11 Gerstein HC, Santaguida P, Raina P, et al. Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. *Diabetes Res Clin Pract* 2007; **78:** 305–12.

12 Saad MF, Knowler WC, Pettitt DJ, Nelson RG, Mott DM, Bennett PH. The natural history of impaired glucose tolerance in the Pima Indians. *N Engl J Med* 1988; **319:** 1500–06.

13 Wu Z, Yao C, Zhao D, et al. Sino-MONICA project: a collaborative study on trends and determinants in cardiovascular diseases in China, Part i: morbidity and mortality monitoring. *Circulation* 2001; **103:** 462–68.

14 He J, Gu D, Wu X, et al. Major causes of death among men and women in China. *N Engl J Med* 2005; **353:** 1124–34.

15 Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. *JAMA* 2003; **290:** 486–94.

16 Chiasson JL. Acarbose for the prevention of diabetes, hypertension, and cardiovascular disease in subjects with impaired glucose tolerance: the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) Trial. *Endocr Pract* 2006; suppl 1: 25–30.

17 Knowler WC, Sartor G, Melander A, Schersten B. Glucose tolerance and mortality, including a substudy of tolbutamide treatment. *Diabetologia* 1997; **40:** 680–86.

18 Rubin RR, Fujimoto WY, Marrero DG, et al. The Diabetes Prevention Program: recruitment methods and results. *Control Clin Trials* 2002; **23:** 157–71.

19 Holloszy JO. Exercise-induced increase in muscle insulin sensitivity. *J Appl Physiol* 2005; **99:** 338–43.

20 Writing Team for the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group. Sustained effect of intensive treatment of type 1 diabetes mellitus on development and progression of diabetic nephropathy: the Epidemiology of Diabetes Interventions and Complications (EDIC) study. *JAMA* 2003; **290:** 2159–67.

21 Hamman RF, Wing RR, Edelstein SL, et al. Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care* 2006; **29:** 2102–07.

22 International Diabetes Federation. Diabetes Atlas, Third Edition, 2006. http://www.eatlas.idf.org/media/ (accessed Aug 4, 2008)

23 Wu YF. Overweight and obesity in China. *BMJ* 2006; **333:** 362–63.

24 Roglic G, Unwin N, Bennett PH, et al. The burden of mortality attributable to diabetes: realistic estimates for the year 2000. *Diabetes Care* 2005; **28:** 2130–35.