Original Article

An integrated intervention program to control diabetes in overweight Chinese women and men with type 2 diabetes

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This study evaluated a structured and integrated intervention program on diabetes management in individuals with type 2 diabetes in Shanghai, China. Men and women with type 2 diabetes and body mass index $\geq$ 23 kg/m^2 were randomized into a 24-week, prospective, randomized clinical trial. The Reference Group (n=50) received diabetes education including diet and physical activity instruction only; the Intervention Group (n=100) received more intensive intervention, including diabetes education with frequent blood glucose monitoring, nutritional counseling, meal plans with diabetes-specific nutritional meal replacement, and weekly progress updates with study staff. Major study assessments were obtained at baseline, and after 12 and/or 24 weeks of intervention. The Intervention Group improved fasting blood glucose, insulin, systolic and diastolic blood pressures compared to Reference Group (p<0.05). Importantly, HbA1c was lower (p<0.001) in the Intervention Group at 12 weeks (-0.6 ± 0.1%) and 24 weeks (-0.8 ± 0.1%). Weight loss was modest, but significant differences were observed between groups (p<0.05). Weight change from baseline after 12 and 24 weeks was -2.8 ± 0.2% and -3.7 ± 0.3%, respectively, in the Intervention Group vs -1.8 ± 0.4% and -2.5 ± 0.4% in the Reference Group. Additionally, waist and hip circumferences and waist:hip ratio decreased in the Intervention compared to the Reference Group (p<0.05). In conclusion, this study demonstrates that Chinese men and women with type 2 diabetes following an integrated intervention program including diabetes education, frequent blood glucose monitoring and daily use of a diabetes-specific meal replacement, can achieve significant improvements in glycemic control and markers of cardiovascular health.

Key Words: Type 2 diabetes, Diet therapy, Formulated food, Glycosylated hemoglobin, Metabolic syndrome X

INTRODUCTION

Over the past decade, the number of people in China with diabetes has increased dramatically. The prevalence of type 2 diabetes (T2DM) increased from 4.6% in 1995 to 6.4% in 2002 among large urban cities, and from 3.4% to 3.9% in middle and small cities.[1] The World Health Organization predicts that the number of diabetes patients in China will reach 37.6 million by 2025, raising the total number of people with diabetes to one of the largest in the world, second only to India.[2] Diabetes has become a heavy burden to public health and negatively impacts quality of life for individuals and productivity for employers.[3]

Diabetes is a progressive disease, requiring regular medical care and tremendous patient self-management to prevent acute complications and to reduce the risk of long-term complications. Structured interventions including health education and careful attention to diet play an important role in achieving and maintaining better metabolic control. Studies such as the United Kingdom Prospective Diabetes Study have shown that optimal control of blood glucose, lipids and blood pressure can decrease and delay the complications of diabetes.[4] To achieve optimal control of this complex and chronic disease, a multi-

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factored team approach towards diabetes management is recommended by most diabetes associations.[5-7]

Evidence-based research also has demonstrated that medical nutritional management can help to achieve and maintain better metabolic control in individuals with diabetes.[8] Specifically, trials using meal replacements designed for those with T2DM have demonstrated significant weight loss with abdominal fat reduction and improvements in HbA1c, fasting blood glucose, and reductions in the need for hypoglycemic medications.[9-11] These studies, however, have been carried-out mainly in countries in which individuals follow a traditional Western diet. Studies utilizing meal replacements have not been conducted in individuals with T2DM in China.

The present study was designed to evaluate the effectiveness of a structured diabetes intervention, including diabetes education and nutritional counseling, meal plans with diabetes-specific nutritional meal replacement, and scheduled glucose monitoring, on diabetes control and management in individuals with T2DM in China.

MATERIALS AND METHODS

Study Design

This study was designed as an un-blinded, randomized, controlled clinical trial. All participants were recruited from employees of Shanghai Turbine Company, Electric Machinery Company and Huadong Hospital, Shanghai, China. The study protocol was designed in the U.S. and approved by the Institutional Review Board of Huadong Hospital. All participants provided written informed consent before being enrolled into the study.

Inclusion criteria included men and women 18-70 years of age, diagnosed with T2DM, and body mass index (BMI) $\geq$ 23 kg/m^2. Subjects were excluded from the study if they were pregnant, taking medications or supplements for weight loss, had advanced diabetes complications, taking insulin, or had a recent history of a cardiovascular event, cancer, or other chronic disease that might interfere with participation.

At baseline, information on demographic characteristics, dietary intake, physical activity, medical history, health habits and physical activity level were collected using a Know Your Number® questionnaire (BioSignia, Inc., North Carolina, USA); dietary information was collected using a 24 hour recall and a short version of food frequency questionnaire; and a health and productivity questionnaire was also administered at beginning and end of the study. Physical examinations were conducted at baseline, midpoint (12 week) and endpoint (24 week), including body weight, waist and hip circumference, and blood pressure. Fasting blood samples were collected at all three time points, and glucose, HbA1c, blood lipids and other biomarkers were analyzed at Huadong Hospital laboratory.

Eligible subjects were randomly assigned to the Intervention (n=100) or Reference (n=50) Groups. Subjects in the Reference Group received diabetes education including diet and physical activity instruction only, while those in the Intervention Group also received additional diabetes intervention (described below) including scheduled glucose monitoring, meal plans including a diabetes-specific nutritional meal replacement, and group diabetes education.

Diabetes Intervention

All study participants were provided diabetes education materials used for monthly group lectures lead by experienced nutritionists from Huadong Hospital. Participants received information on diabetes management, behavioral and lifestyle modification, physical activity, and other diabetes-related health care information, following *"Diabetes A-Z,"* an American Diabetes Association publication, 3rd edition, (Peking University Medical Center Press, Beijing, China). Additionally, subjects received healthy eating instruction (with sample meal plans) including concepts and applications of food exchanges and low-glycemic foods, based on American Diabetes Association and Chinese Diabetes Association guidelines.

Participants in the Intervention Group also attended weekly sessions at their respective worksites. For each session, lasting approximately 30 minutes, participants met with a research dietitian for diet consultations and a study physician from the company clinic for medical evaluation including assessment of adverse events, a review of blood glucose measurements and adjustment of medications, if necessary. Subjects in the Intervention Group also were provided with blood glucose monitors (Optium™, Medisense, Abbott Diabetes Care, Alameda, CA) and accessories to encourage frequent testing. To facilitate adherence to the healthy eating plan, participants in the Intervention Group were also provided with a low glycemic,[12] diabetes-specific nutritional meal replacement (Glucerna® SR, Abbott Laboratories, Chicago, IL) that they used to replace breakfast food items such as milk, soymilk, rice soup, or congee at the morning meal. The nutrient profile of the nutritional meal replacement is outlined in Table 1. Cans of powdered formula were pro-

Table 1. Composition of diabetes-specific nutritional supplement.†

	45 g wt serving (230 mL fl oz)
Energy	200 kcal
Protein	10 g (20% energy)
Fat	7 g (33% energy)
Saturated fatty acids	0.5 g (2.6% en)
Monounsaturated fatty acids	3.3 (15% en)
Carbohydrate	25 g (47% energy)
Sugars	7 g
Total Dietary fiber	3 g
Glycemic Index‡	30

† Nutritional supplement ingredients: Protein blend (caseinates), Fat blend (high oleic sunflower oil, soy oil), carbohydrate blend (resistant maltodextrin, corn maltodextrin, fructose, maltitol); vitamin and mineral premixes.

‡ Glycemic index was measured using valid scientific methodology at the University of Sydney, Glycemic Index Research Service, Human Nutrition Unit, Department of Biochemistry, Sydney, Australia.

vided weekly; participants recorded daily intake on clinical record forms. Compliance to the product intake was assessed weekly by the return of empty formula containers and review of the product intake forms by the study dietitians at each weekly counseling session.

Study Assessments

The study duration was 24 weeks, and major study outcomes were obtained at baseline, 12 and 24 weeks. The primary study outcome was body weight which was assessed with lightweight clothing and without shoes, as was height at baseline. Blood pressure was assessed using a mercury sphygmomanometer. Waist circumference was measured midway between the spina iliaca superior and the lower rib margin. Hip circumference was measured at the widest point over the buttocks. Two independent trained members of the study staff completed these measurements with a mean difference between observers of < 1 centimeter.

Blood samples were collected via venipuncture after an overnight fast (i.e., no food or drink except water for 8 hours). Subjects were instructed to withhold medications prior to blood draws. Plasma glucose, insulin and lipids were assessed using a Roche Automatic Analyzer modular P800 (Roche Diagnostics GmbH, Mannheim, Germany). Measurements of HbA1c were assessed with immunosuppressive turbidimetry assay using Hitachi Automatic Analyzer 7600-010 (Medical System, Suzhou, China).

Nutrient intakes were assessed using 24-hour dietary recall, a food frequency questionnaire (FFQ), and a food change questionnaire (FC). The 24-hour dietary recall was obtained by research dietitians, and nutrient intakes from the dietary recalls were calculated using a computerized food analysis system (SY Software, developed in the School of Public Health, Fudan University, Shanghai, China). Additional information about participants' food choices was obtained using FFQ and FC questionnaires which were developed by experienced nutritionists from the Clinic Nutrition Center at Fudan University based on Chinese food habits and validated based on frequently used food in the Shanghai area.[13] For simplicity, the FFQ included a list of 18 common foods and beverage categories, including over 150 individual food items. For example, selections for rice frequency were: "3 times per day," "2 times per day," "once a day", "every other day," "and 1 to 2 times a week." The unit of intake was "liang" (one liang = 50 grams). For the FC questionnaire, participants indicated the changes of main food intake from beginning to end of the study; participants were asked to compare their current diet to that before they enrolled by marking "increase" "decrease" or "no change" for 17 food category/preparation choices. Change amount was required to be at least 1 serving increase or decrease daily. Many of the food categories for the FFQ and FC differed between questionnaires making comparisons difficult; therefore, these data are used for descriptive qualitative purposes and not for survey cross-validation.

The health and productivity burden due to T2DM was assessed using a simplified 44 question /106 item questionnaire administered using paper/pencil format at baseline and after 24 weeks. The questionnaire included items to assess the severity of diabetic symptoms, general physical and mental health status, work limitations and productivity, and knowledge gaps related to diabetes self-care. The questionnaire was a combination of proven and validated items from the Work Limitations Questionnaire (WLQ),[14] and Short Form 36 (SF-36),[15] along with additional questions to assess the burden of disease and the impact of the treatment. The survey was developed in the US (Harris-Allen Group, Brookline, Massachusetts, USA). When available, the Chinese language version was used; otherwise, the questionnaires were translated by the principal investigators with adjustment according to the Chinese culture.

Statistical Analyses

Descriptive statistics were prepared for the values at baseline, 12 and 24 weeks, as well as the differences from baseline to 12 and 24 weeks, and the percent changes from baseline to 12 and 24 weeks. The primary objective of the analyses was to compare the two study groups. Baseline and FC and FFQ comparisons were made using Student's t-tests or chi-square analyses. Repeated measures analysis of covariance (mixed model) was used to compare the groups for the continuous outcomes. If there were a significant Week by Group interaction, between-group comparisons were made at 12 and 24 weeks. Anthropometric data were analyzed including a factor for gender. The Metabolic syndrome (MetS) was analyzed by Generalized Estimating Equations of binary data. Results were statistically significant when $p<0.05$. The data analysis was generated using SAS/STAT software, Version 9.1.3, of the SAS system for Windows (SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline Characteristics and Study Participation

Key metabolic and other general characteristics of the study participants at baseline are shown in Table 2. The groups were closely matched; subjects were predominantly male, overweight or obese, in relatively good glycemic control having a mean HbA1c of approximately 7%, with an average duration of diagnosed diabetes of four years. As expected, the majority of participants in both groups met the ethnicity-specific criteria for the MetS.[16] Approximately one third of the participants had attended some college or graduate school, and the subjects' occupations varied from office clerical, to professional (e.g., pharmacist) and technical (e.g., machine operator) categories. The differences between groups included higher total cholesterol in the Reference Group, and a greater proportion of smokers at baseline in the Intervention Group ($p<0.05$). In addition, females in the Intervention Group tended to have larger waist and smaller hip circumferences; as a result, the waist:hip ratio was significantly greater for females in the Intervention Group at baseline.

The retention rate was high – only four subjects withdrew prior to study completion (n=3 in Intervention Group; n=1 in Reference Group). The reasons for withdrawal included: interference with work schedule (n=2); changed in job (n=1) and gastrointestinal discomfort (diarrhea) associated with nutritional supplement consumption (n=1).

Table 2. Baseline Characteristics of Study Participants Randomized to Intervention and Reference Groups.

	Intervention Group (n=100)	Reference Group (n=50)	Between-Group P value
Gender (Female/Male)	26% / 74%	32% / 68%	0.440†
Age, years	51 ± 1	51 ± 1	0.704‡
Duration of Diabetes, years	4 ± 0.3	4 ± 0.4	0.499‡
HbA1c, %	7.1 ± 0.1	7.0 ± 0.2	0.637‡
Fasting Glucose, mmol/L	8.2 ± 0.3	8.7 ± 0.4	0.374‡
Fasting Insulin, μIU/mL	25 ± 1	32 ± 4	0.133‡
Systolic Blood Pressure, mm Hg	131 ± 1	135 ± 2	0.130‡
Diastolic Blood Pressure, mm Hg	87 ± 2	89 ± 2	0.256‡
Total Cholesterol, mmol/L	4.8 ± 0.1	5.2 ± 0.2	0.022‡
LDL Cholesterol, mmol/L	2.9 ± 0.1	2.9 ± 0.1	0.804‡
HDL Cholesterol, mmol/L	1.2 ± 0.0	1.3 ± 0.0	0.564‡
Triglycerides, mmol/L	2.2 ± 0.1	3.2 ± 0.5	0.062‡
Body Mass Index (kg/m^2) §	26.6 ± 0.3	27.2 ± 0.3	0.102
Weight, kg§	75.6 ± 1.1	75.7 ± 1.0	0.561
Waist circumference, cm§	92 ± 1	91 ± 1	0.629
Hip circumference, cm§	97 ± 1	98 ± 1	0.099
Waist:Hip ratio, males§¶	0.95 ± 0.01	0.95 ± 0.01	0.970
Waist:Hip ratio, females§¶	0.93±0.01	0.88±0.01	0.004
Metabolic Syndrome††	75%	76%	0.894†
On anti-hyperglycemic medications	85%	79%	0.407†
Traditional Chinese medications for diabetes management	6%	8%	0.643†
Diagnosed with Hypertension	49%	54%	0.564†
On anti-hypertensive medications	47%	47%	0.994†
Education			0.791†
Middle School	28%	33%	
High or Technical School	36%	33%	
College	35%	31%	
Graduate	2%	4%	
Current Smoker	54%	36%	0.038†
Engages in some/modest physical activity	52%	50%	0.861†

Values are means ± SEM. †Chi-square test. ‡Two-sample t-test . § Anthropometrics were analyzed using a two-factor analysis of variance with group, gender and group by gender interaction. ¶Significant gender x group interaction for waist:hip. ††Metabolic Syndrome (MetS) defined (reference 16) as having three or more of the following: waist circumference (ethnicity specific) male ≥90 cm; female ≥ 80 cm); triglycerides > 1.7 mmol/L; HDL cholesterol <1.29 mmol/L; systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg; fasting plasma glucose ≥5.6 mmol/L.

Changes in Metabolic Parameters and Body Composition

Changes in glycemic and cardiovascular parameters and body composition are shown in Table 3. Both groups showed some improvement in fasting blood glucose and insulin at 12 weeks but the changes were sustained in the Intervention Group at 24 weeks and significantly different compared to the Reference Group. Mean fasting blood glucose values at 24 weeks were 7.4 ± 0.2 vs 8.9 ± 0.4 mmol/L (p<0.001), Intervention vs Reference, respectively. Consequently, HbA1c also significantly improved in the Intervention vs Reference Group. Figure 1 shows that mean HbA1c was essentially unchanged in the Reference Group while in contrast, mean HbA1c was lower in the Intervention Group at both 12 and 24 weeks.

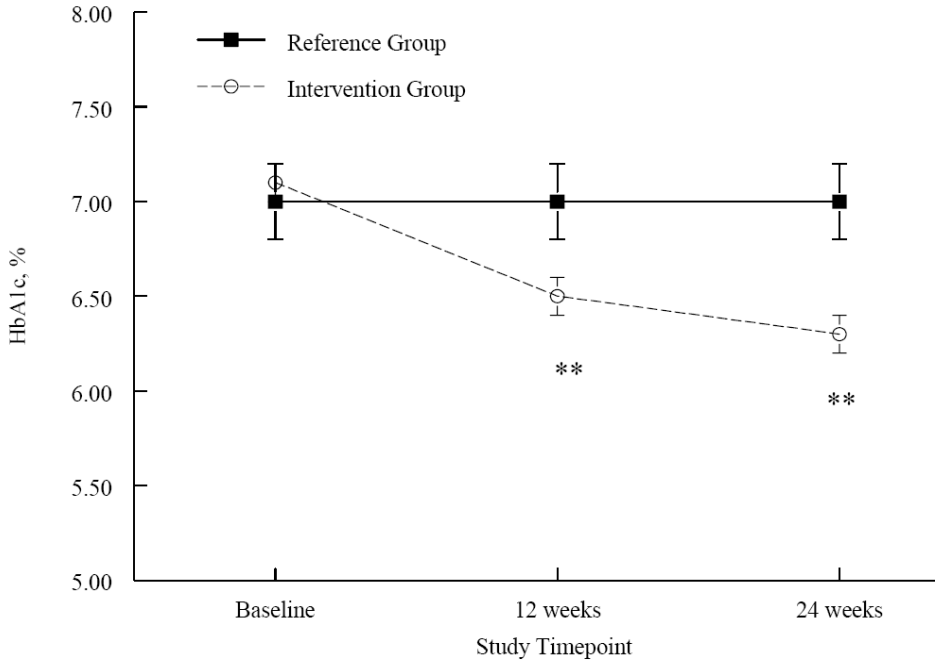

Figure 1. HbA1c (%; mean ± SEM), at 12 and 24 weeks. ** $p<0.001$.

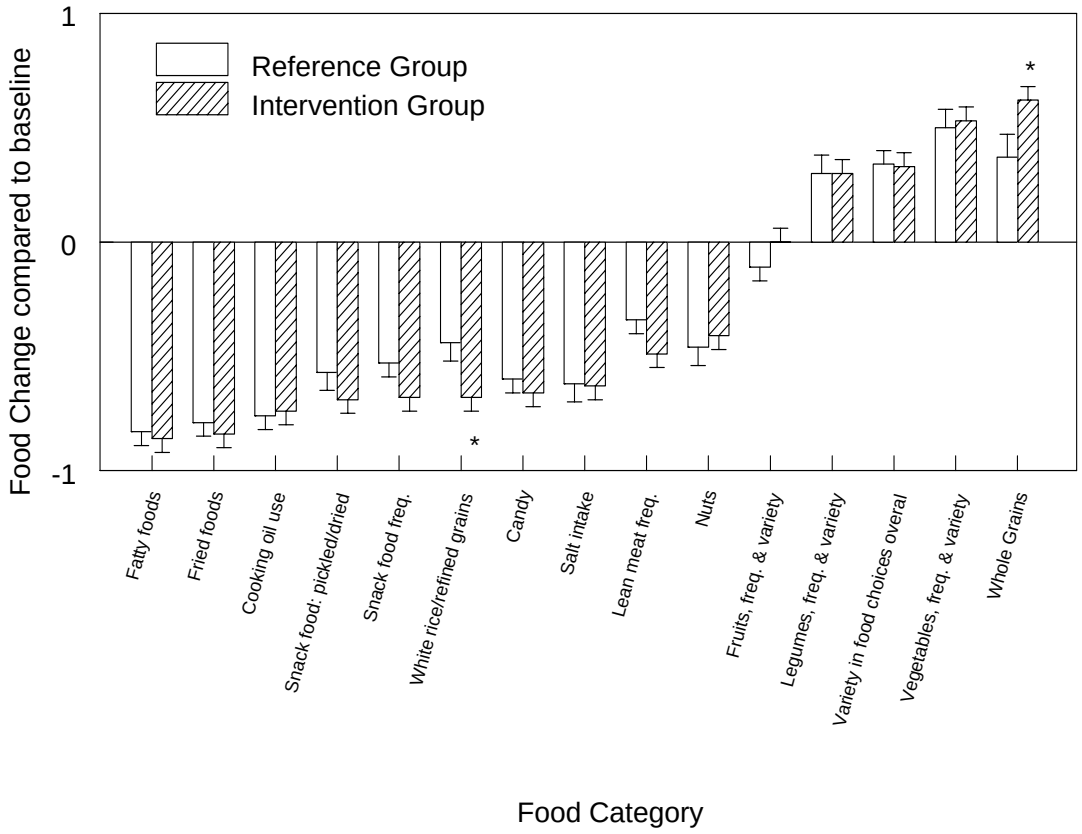

Figure 2. Change in food category intake at 24 weeks compared to baseline in Reference Group, (clear bar), and Intervention Group (diagonal bar). Values indicate mean change score (± SEM), where –1= decrease, 0 = no change, +1 = increase, for each category/preparation choices; change amount was required to be at least 1 serving increase or decrease daily; * $p<0.05$.

Mean systolic blood pressure improved and was lower in the Intervention Group compared to the Reference at 24 weeks (124 ± 1 vs 133 ± 2 mm Hg, $p<0.01$, Intervention vs Reference). Diastolic blood pressure also improved in the Intervention Group (at 24 weeks, 84 ± 1 vs 89 ± 1 mm Hg, $p<0.01$, Intervention vs Reference). With the exception of a small reduction in HDL Cholesterol in

Table 3. Changes in Metabolic Parameters and Body Composition

Outcome	Wk	Intervention Group	Reference Group	Overall Between-Group *p* value	Between-Group *p* value
Glycemic Control					
Glucose (mmol/L)	12	-1.3 ± 0.3	-1.0 ± 0.4	--†	0.045
	24	-0.9 ± 0.3	0.2 ± 0.4		<0.001
Insulin (μIU/mL)	12	-2.7 ± 1.3	-6.2 ± 2.5	--†	0.571
	24	-3.6 ± 1.4	-0.4 ± 3.1		0.011
HbA1c (%)	12	-0.6 ± 0.4	0.1 ± 0.1	--†	<0.001
	24	-0.8 ± 0.1	0.1 ± 0.2		<0.001
Blood pressure (mm Hg)					
Systolic	12	-6.7 ± 1.4	-4.9 ± 2.1	--†	0.140
	24	-7.5 ± 1.3	-1.7 ± 1.9		<0.001
Diastolic	12	-3.6 ± 1.1	-1.7 ± 1.9	0.005	
	24	-3.4 ± 1.0	-0.1 ± 1.7		
Blood Lipids (mmol/L)					
Total Cholesterol	12	-0.0 ± 0.1	-0.3 ± 0.1	0.834	
	24	-0.1 ± 0.1	-0.2 ± 0.1		
LDL Cholesterol	12	-0.3 ± 0.1	-0.3 ± 0.1	0.264	
	24	-0.3 ± 0.1	-0.2 ± 0.1		
HDL Cholesterol	12	-0.1 ± 0.0	-0.2 ± 0.0	0.035	
	24	-0.1 ± 0.0	-0.2 ± 0.0		
Triglycerides	12	-0.1 ± 0.1	-0.8 ± 0.4	0.774	
	24	0.2 ± 0.2	-0.5 ± 0.6		
Body Composition‡					
Weight (kg)	12	-2.1 ± 0.2	-1.3 ± 0.3	0.040	
	24	-2.7 ± 0.2	-1.8 ± 0.3		
BMI (kg/m2)	12	-0.7 ± 0.1	-0.5 ± 0.1	0.052	
	24	-1.0 ± 0.1	-0.7 ± 0.1		
Waist circumference (cm)	12	-2.2 ± 0.4	1.7 ± 0.5	<0.001	
	24	-3.4 ± 0.3	0.1 ± 0.7		
Hip circumference (cm)	12	-1.4 ± 0.2	0.3 ± 0.4	0.003	
	24	-2.7 ± 0.3	-2.0 ± 0.4		
Waist:Hip ratio	12	-0.9 ± 0.4	2.2 ± 0.5	<0.001	
	24	-1.0 ± 0.3	2.3 ± 0.6		
Metabolic Syndrome§	12	62%	86%	0.009	
	24	67%	84%		

Values are means ± SEM. †Overall group comparison not applicable due to significant Week by Group interaction. ‡Anthropometric measures were analyzed also including a factor for gender. § Metabolic Syndrome (MetS, % of subjects) defined as in reference (16); see legend Table 2.

the Reference Group (Table 3), there were no differences in blood lipids between groups.

Overall, weight loss was modest; however, there was a significant difference between groups over the study period ($p<0.05$). These changes represented a –1.8 ± 0.4% and –2.5 ± 0.4% reduction at each time point for the Reference Group and a –2.8 ± 0.2% and –3.7 ± 0.3% reduction at each time point for the Intervention Group. As a result, BMI improved in the Intervention Group ($p=0.052$). Waist and hip circumference decreased in the Intervention Group after 12 and 24 weeks. The waist:hip ratio also decreased in the Intervention group compared to the Reference Group. Consistent with these improvements, a reduction in the prevalence of individuals characterized as having the MetS was observed in the Intervention Group compared to the Reference Group. The apparent increase in the MetS in the Reference Group compared to baseline can be attributed to a combination of worsening of meta-

Table 4. Macronutrient Intakes from 24 hour recall.

		Intervention	Reference	Between-Group *p* values
Energy, kcal	Baseline	1858 ± 47	1829 ± 61	0.711†
	12 wks	1781 ± 32	1806 ± 63	0.634‡
	24 wks	1606 ± 36	1602 ± 43	
Carbohydrate, % kcal	Baseline	50 ± 0.8	49 ± 1.1	0.746†
	12 wks	52 ± 0.6	51 ± 1.1	0.341‡
	24 wks	46 ± 0.7	45 ± 1.1	
Protein, % kcal	Baseline	17 ± 0.3	17 ± 0.4	0.407†
	12 wks	19 ± 0.3	16 ± 0.5	<0.001‡
	24 wks	20 ± 0.4	18 ± 0.5	
Fat, % kcal	Baseline	34 ± 0.5	34 ± 0.8	0.985†
	12 wks	30 ± 0.4	33 ± 0.7	<0.001‡
	24 wks	33 ± 0.4	37 ± 0.8	
Fiber, g	Baseline	6.7 ± 0.4	6.9 ± 0.5	0.649†
	12 wks	8.2 ± 0.3	7.1 ± 0.5	0.010‡
	24 wks	7.4 ± 0.3	6.4 ± 0.5	

Values are means ± SEM. † Two-sample t-test at baseline ‡ Repeated Measures Analysis of Covariance Overall

bolic parameters including waist circumference, HDL cholesterol, and blood pressure in certain individuals.

Dietary Intake Assessments

Nutrient intake analysis from 24 hr recall at baseline revealed that on average, participants in both groups consumed a diet averaging 1830-1860 kcals, with 49-50% energy from carbohydrate, 34% energy from fat, and 17% energy from protein (Table 4). Overall, fiber intake was low, averaging <7 g per day. During the 24 weeks, total calories and carbohydrate intake (as % of energy) decreased similarly in both groups. Also during the study, fat intake was higher in the Reference Group, while average protein intake was higher in the Intervention Group. Mean fiber intake also increased modestly, but significantly, in the Intervention Group.

Analysis of the FC and FFQ questionnaires revealed that white rice contributed a large portion of carbohydrate intake in both groups and was eaten at most meals. No differences in intakes were observed between groups at baseline; however, both FC and FFQ revealed a decrease in consumption of white rice/refined grains such as white flour and for FC an increase in consumption of whole grains (e.g., corn, oats, buckwheat, sorghum, pearl barley) in the Intervention vs Reference Group, $p<0.05$ (Figure 2). Another important difference between the Groups included the consumption of the meal replacement in the Intervention Group only [45 g of meal replacement powder (approximately 200 kcal) was consumed daily based on review of participant's diet records].

Disease Burden and Productivity

The Intervention Groups' average score on the diabetes symptom severity checklist, a ten item components of the Health and Productivity survey, was significantly lower than the Reference Groups' average score after 24 weeks (Table 5). Subjects in the Intervention Group significantly increased the frequency of assessing blood glucose levels compared to the Reference Group; based on a five-point scale (0 – 4), the average scores at baseline for both groups, approximately 1.38-1.48, indicated testing frequency between "less than monthly" and "monthly." At the end of the 24 weeks, the average score in the Intervention Group of 3.66 was significantly greater than the Reference Group, which indicated an increased testing frequency of between "weekly" and "daily." The Reference Group scored higher than the Intervention Group on the question related to "Wants more information about diabetes" at baseline; however the difference was not significant at 24 weeks.

There were no differences between groups at baseline in the mean scores (normalized) from the Physical Component Summary (PCS) or the Mental Component Summary (MCS) of the SF-36 questionnaire. However, after 24 weeks, the Intervention Group's PCS scores were significantly higher while the MCS scores were significantly lower than the Reference Group's scores. Scores on the other sub-scales of the Health and Productivity survey were not significantly different between groups (not shown). Both Groups reported lower scores at the end of the study on the Output Work Demands and the WLQ Index of the WLQ-Short Form survey, but there were no significant differences between the groups. Finally, no significant difference in absentee days, total lost days or accidents and injuries were found (not shown).

DISCUSSION

This study demonstrated that Chinese individuals with T2DM who participated in a structured and integrated intervention program conducted within a workplace setting showed significant improvements in parameters associated with glycemic control and markers of cardiovascular health compared to a Reference Group following usual care practices. Consistent with these improvements, the prevalence of the MetS was also significantly reduced in the Intervention Group. Thus, the combination of education, dietary management including a diabetes-specific nutritional meal-replacement, and frequent glucose testing are effective in diabetes management and control in this population.

While it is not possible to attribute the study outcome to any single component of the intervention, it is widely

Table 5. Disease Burden and Productivity Scores

	Study Time-point	Intervention	Reference	Between-Group *p* value
Diabetes Symptom Severity Score	Baseline	17.9 ± 1.6	16.2 ± 1.7	0.462†
	24 wks	13.7 ± 1.4	17.1 ± 1.6	0.050‡
Frequency of Blood Glucose Checks	Baseline	1.38 ± 0.09	1.48 ± 0.14	0.189†
	24 wks	3.66 ± 0.07	1.78 ± 0.13	<0.001‡
Feels in Control of Diabetes	Baseline	75.9 ± 1.3	73.4 ± 2.1	0.284†
	24 wks	77.3 ± 1.0	73.7 ± 1.7	0.091‡
Wants more information about diabetes	Baseline	65.9 ± 2.7	75.6 ± 3.3	0.034†
	24 wks	47.6 ± 2.6	58.4 ± 3.8	0.068‡
PCS of SF 36	Baseline	50.1 ± 0.4	49.2 ± 0.6	0.266‡
	24 wks	51.4 ± 0.4	48.9 ± 0.8	0.004‡
MCS of SF 36	Baseline	51.6 ± 0.6	52.3 ± 1.1	0.600†
	24 wks	51.0 ± 0.7	53.8 ± 0.9	0.017‡
Output Work Demands WLQ short form	Baseline	12.0 ± 2.6	9.3 ± 2.6	0.454†
	24 wks	5.5 ± 1.5	7.3 ± 2.5	0.485‡
Output Work Index WLQ Index	Baseline	6.9 ± 0.4	6.6 ± 0.6	0.688†
	24 wks	5.9 ± 0.3	6.0 ± 0.5	0.830‡

Values are means ± SEM. † Two-sample t-test ,‡ Analysis of Covariance, PCS (physical component summary); MCS (mental component summary); WLQ (work limitations questionnaire).

accepted that weight reduction can improve insulin sensitivity and metabolic parameters in T2DM.[5] Studies have shown that mild to moderate weight loss of 5 to 10% can improve diabetes control even if desirable weight is not achieved.[5,9] Although weight loss during the present 24 week study was modest and averaged <5% in both groups, a reduction in waist circumference measures and/or waist: hip ratio may be most responsible for the overall metabolic improvements in the Intervention Group. The mean reduction in waist circumference in the Intervention Group at 6 months is consistent with the magnitude of reduction (>3 cm), shown to improve metabolic risk factors in Asian men.[17] Of interest is the observation of a modest decrease in body weight with an apparent increase in waist:hip ratio in the Reference Group. Because these changes were not associated with metabolic improvements, it is likely that they reflect compositional changes (e.g., shifting in body fluids), unrelated to a reduction in abdominal fat.

It is also likely that reduction in total and abdominal weight combined with other components of the structured intervention helped patients participating in the intervention arm achieve improvements in glycemic and metabolic control. An integrated approach to diabetes management such as that used in the present study can have a substantial impact on awareness and behavior and thus control of the metabolic condition. For example, a recent study in adult subjects who were predominantly T2DM conducted in the U.S. showed that the gain in knowledge of the targets of diabetes care after receiving diabetes self-management education can predict the achievement of target HbA1c levels after 6 months.[18] The authors concluded that the education improved patients' understanding of the importance of reaching the targets, thus motivated them to adopt better self-management practices leading to better glycemic control. During the time this current study was conducted, home blood glucose monitoring was not a common practice (Dr. Wang, personal communication, September, 2007). A review of study records showed that subjects in the Intervention Group increased self-monitoring of blood glucose throughout the 24-week intervention period. An increase in the frequency of blood glucose testing in the group that received glucose monitors no doubt contributed to a greater awareness of the impact of their daily behaviors on their blood glucose, thus leading to important changes to enable better control of their condition.

Changes in diet quality of the study participants also likely contributed to the observed improvements. Participants in both groups reduced intakes of total calories and carbohydrates; however, the Intervention Group reported significantly greater reductions in intakes of white rice and other refined grains while the intake of whole grains increased. White rice and other refined grains elicit a significant postprandial glycemic response,[19,20] while whole grains have a lower glycemic index and provide other important nutrients, such as selenium, potassium, magnesium and fiber. High intake of foods with a high glycemic index and glycemic load, especially rice, the main carbohydrate-contributing food in this population, has been reported to increase the risk of T2DM mellitus in Chinese women.[21] In contrast, replacing high-glycemic foods with lower glycemic alternatives has been shown to improve glycemic control and HbA1c in an Asian population.[22] Although the mechanisms are not completely understood, meals having a lower glycemic response contribute to improved post meal and diurnal glucose profiles in subjects with T2DM and insulin resistance.[23] Post-meal blood glucose levels have been proven to be an important part of overall glycemic control, particularly in patients having HbA1c <7.3%.[24] Additionally, effects of low glycemic diets on hormones such as those secreted by the gut (e.g., glucagon-like peptide1, peptide YY, cholecystokinin) may also contribute to body weight and/or body fat com-

position and metabolic improvements.[25] Furthermore, there may have been an added benefit of daily consumption of the low glycemic diabetes-specific nutritional meal replacement, thus contributing to the overall quality of the dietary intervention. A review and meta-analysis of diabetes-specific formulas showed that they can contribute to improved HbA1c.[8] Participants in the present study were in relatively good glycemic control at the study onset; thus, the changes in overall diet composition, including high compliance with the nutritional meal replacement, would be expected to contribute to the striking improvements in HbA1c and the prevalence of the MetS in the Intervention Group.

Finally, there may have been changes in other medical or self-management behaviors that were not evaluated which may have contributed to the improvements. For example, although subjects were not instructed to adopt a formal exercise program, and thus daily exercise was not tracked, it is possible that many did increase regular physical activity after receiving education. In addition, because this was an un-blinded study in a worksite setting, it is possible that individuals in the Intervention Group shared information amongst co-workers that could have affected some of the study endpoints. Another possible factor affecting the observed changes could have been changes to diabetes medications. A review of subject records for the Intervention Group revealed that n=22 (or 22%) of participants had a decreased need for anti-hyperglycemic medications (frequency, number or dose) during the 24 week intervention. In contrast, only n=7 (or 7%) had an increased need for anti-hyperglycemic medications. Thus, it is unlikely that an increase in medications contributed substantially to the average reductions in HbA1c in the Intervention Group. Due to the nature of the study design, detailed information on medication usage during the study was not collected from the Reference Group participants.

While improvement in HbA1c and the prevalence of the MetS are the primary goals of diabetes management intervention, improvements in patient self-reported outcomes also have value. In this study a nine-item subset of the SF-36 was used to generate both PCS and MCS as part of the Health and Productivity Questionnaire. Although there were statistically significant differences between the scores for the Intervention and Reference Group at the end of the treatment, neither is clinically significant.[26] The Diabetes Symptom Severity Checklist was included to capture some of the unpleasant symptoms and physical side effects experienced by people trying to manage their diabetes such as lightheadedness, neuropathy pain, frequent urination, or response to hypoglycemic episodes. All of these symptoms can be improved by better diabetes management and maintaining glucose at a normal level. A reduction in the frequency of these types of symptoms results in lower scores on the checklist. Although the Group's were significantly different, based on the scale used, neither the Intervention nor Reference Group appeared to be excessively bothered by these types of symptoms at baseline or at the end of the study.

A limitation of the questionnaires used in the study is that many questions were based on those developed for a Western population and had never been tested for use in a Chinese population. As such, it is possible that participants may have had some difficulty in providing undesirable self-reported responses (Dr. Wang, personal communication, September, 2007). Although the scores on the Output Work Demands subscale of the WLQ-short form decreased in both groups over the course of the study, there were no statistically significant differences. It may not be surprising that no improvement in productivity was detected because both groups of subjects were functioning at fairly high levels based on their high scores on the PCS and MCS scales and low scores on the Diabetes Severity Symptom Checklist. Studies with participants having more severe diabetes symptoms might be needed to see measurable improvements in productivity.

In summary, Chinese individuals with T2DM who participated in a structured intervention program showed significant improvements in metabolic parameters associated with glycemic control and cardiovascular health risk factors compared to a Reference Group following usual care practices. Consistent with these improvements, the prevalence of the MetS was also significantly reduced. Thus, the combination of education, dietary management including a diabetes-specific nutritional meal-replacement, and frequent glucose testing can be effective in diabetes management and control in this patient population.

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Original Article

An integrated intervention program to control diabetes in overweight Chinese women and men with type 2 diabetes

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中国男性和女性超重 2 型糖尿病控制综合干预研究

本研究是针对中国上海地区 2 型糖尿病患者进行的结构化综合干预。对体质指数（BMI）≥ 23 kg/m^2 的男性和女性 2 型糖尿病患者进行为期 24 周的前瞻性随机临床试验，对照组（n＝50）仅接受包括饮食和运动指导在内的普通糖尿病教育，干预组（n＝100）则接受更多的干预措施，包括糖尿病教育、营养咨询、经常性血糖监测、糖尿病专用的膳食替代食物，以及研究人员每周与其进行面对面的个体化饮食指导与随访。主要的研究资料在基线、12 周和/或 24 周收集完成。与对照组相比，干预组的空腹血糖、收缩压和舒张压得到明显改善（p<0.05）。尤其重要的是，干预组的糖化血红蛋白（HbA1c）水平在第 12 周（-0.6±0.1%）和第 24 周（-0.8±0.1%）明显下降，p<0.001。体重有轻度下降，干预组体重变化在 12 周和 24 周后（-2.8±0.2% ，-3.7±0.3%）与对照组体重均值的变化（-1.8±0.4%，-2.5± 0.4%）相比，差异有显著性 p<0.05。此外，与对照组相比，干预组的腰围和腰臀比明显下降（p<0.05）。结论：本研究表明，对中国男性和女性 2 型糖尿病患者进行综合干预，包括饮食指导、糖尿病教育、经常性的血糖监测以及每日使用糖尿病专用配方作为膳食替代食物，可以达到显著改善血糖控制和心血管健康的作用。

关键词： 2 型糖尿病，饮食治疗，糖尿病专用配方食物，糖化血红蛋白，代谢综合症