# Diet , lifestyle and type 2 diabetes in China

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## Abstract

*Background*

Over the past two decades, China has been undergoing rapid socio-economic and nutrition transitions. Along with these transitions, chronic non-communicable diseases, such as obesity and type 2 diabetes, are becoming serious public health problems. However, only few studies on determinants of type 2 diabetes, such as fetal exposure, dietary patterns, physical activity, and obesity, have been carried out in China.

*Method*

The 2002 China National Nutrition and Health Survey (CNNHS), which is a nationally representative cross-sectional survey, was the source of data for this study. Body weight, height, and fasting blood glucose levels were measured by trained technicians and persons whose fasting glucose was >5.5 mmol/l were given an oral glucose tolerance test. Information on food intake was collected using the 24h recall method for three consecutive days. The amounts of cooking oil and condiments consumed during the three survey days were obtained using a food weighing method. A semi-quantitative food frequency questionnaire was used to investigate the usual diet of persons aged above 14 years in the year before the study. Information on physical activity was collected by trained investigators using a 1-year recall physical activity questionnaire.

*Result*

Central obesity is a better predictor of the presence of glucose tolerance abnormalities than BMI. The optimal cut-off value for waist to height ratio (WHtR) was 0.5, and the prevalence ratio (PR) for this cut-off was 2.85 (95% CI 2.54, 3.21) for men and 3.10 (95% CI 2.74, 3.51) for women.

Dietary patterns and are associated with the presence of glucose tolerance abnormalities in China. Persons in the 'Green Water' dietary pattern had the lowest prevalence of glucose tolerance abnormality (3.9%). Persons in the 'Yellow Earth' dietary pattern (PR 1.22, CI: 1.04–1.43) and the 'New Affluence' dietary

pattern (PR 2.05 CI: 1.76–2.37) had significantly higher prevalence rates than the 'Green Water' dietary pattern.

A high fat/protein–low carbohydrate diet score was associated with a higher prevalence of type 2 diabetes in the Chinese population. The odds ratio comparing the highest with the lowest quintile was 2.75 (95% CI: 2.09–3.61). The odds ratio was 1.87 (95% CI: 1.35–2.58) after further adjustment for socioeconomic status and physical activity.

The 'Green Water' dietary pattern was related to the lowest prevalence of metabolic syndrome (MS) (15.9%). Compared to the 'Green Water' dietary pattern, the 'Yellow Earth' and the 'Western/New Affluence' dietary patterns resulted in an odds ratio of 1.66 ( 95% CI: 1.40–1.96) and 1.37 (95% CI: 1.13–1.67), respectively. Physical activity showed a significant interaction with the dietary patterns in relation to MS risk (*P* for interaction = 0.008). Participants with a combination of sedentary activity and a 'Yellow Earth' or a 'Western/New Affluence' dietary pattern both had more than three times (95% CI: 2.8–6.1) higher odds of MS than active persons with a 'Green Water' dietary pattern.

In areas severely affected by famine in 1959–1961, fetal-exposed persons had an increased risk of hyperglycemia compared to non-exposed persons (OR=3.92; 95% CI: 1.64–9.39; *P*=0.002). Also, in severely affected famine areas, fetal-exposed persons who followed a 'Western/New Affluence' dietary pattern (OR=7.63; 95% CI: 2.41–24.1; *P*=0.0005) or had a high economic status in later life experienced a substantially elevated risk of hyperglycemia (OR=6.20; 95% CI: 2.08-18.5; *P*=0.001).

*Conclusion*

The findings in this thesis indicate that early life environment, central obesity, dietary pattern, and physical activity are associated with the risk of diabetes and metabolic syndrome in the general Chinese population. Keeping body weight in the normal range, improving diet quality, and promoting physical activity would be benefitial for Chinese population to prevent diabetes.

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# CHAPTER 1

## General introduction

Yuna He

China has undergone major economic and epidemiological transitions in recent decades. Increasing globalization and East–West exchanges have been accompanied by increasing population movements, changes in food supply, technology transfer, and cultural admixtures. As a result of the rapid economic development in China, the lifestyle and dietary habits of its population have been changing.

## Dietary changes in China

People's dietary quality has improved significantly in China. The energy and protein intake of urban and rural residents is now basically satisfactory, with an average daily energy and protein intake of 2,254 kcal and 66g, respectively, per reference person. There has been a significant increase in the consumption of meat, eggs, and poultry, with an increase in the percentage of high quality protein from animal-based food and soybeans. Compared with the figures in 1992, the percentage of high quality protein in the total protein intake has increased from 24% to 33%, the energy contribution from total fat has increased from 22% to 30%, and the energy contribution from carbohydrates has decreased from 67% to 60% (1). On average, these proportions are within the recommended range, i.e. an upper limit of 30% for the proportion of energy from fat, and a range between 55% and 65% for the energy contribution from cereals (2).

The dietary pattern among urban residents in 2002 was inappropriate to certain extent. The consumption of poultry, meat, and oil/fat was too high, and cereal consumption was relatively low. By 2002, daily consumption of oils/fats among urban residents had increased to 44g from 37g in 1992. The energy contribution from fat, at 35%, exceeded the recommended upper limit. The energy contribution from cereals among urban residents was only 47%, which is significantly lower than the recommended range **(Figure 1.1).**

China is also facing the dual challenge of nutrition deficiency and over-nutrition, the so-called double burden. Malnutrition among children in China's rural areas is still quite high. In 2002, the prevalence of growth retardation and low body weight among Chinese children under the age of 5 was 17.3% and 9.3%, respectively (1). In poor rural areas, these numbers were much higher (29.3% and 14.4%, respectively). Insufficient intake of calcium, iron, vitamin A and other micronutrients remains a common problem in both urban and rural areas in China.

In 2002, the prevalence of overweight in Chinese adults was 22.8%, and the prevalence of obesity was 7.1%; it was estimated that the number of overweight and obese people had reached 200 million and over 60 million, respectively,

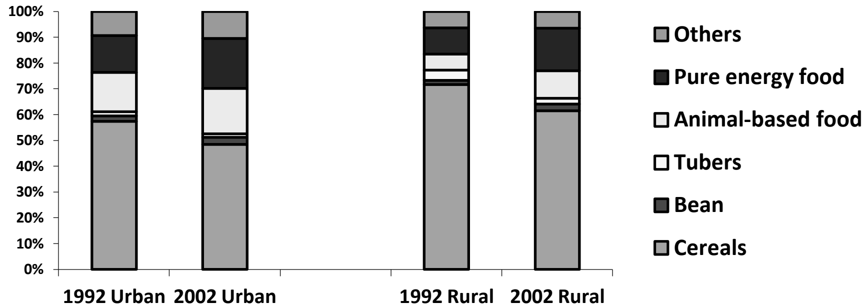


**Figure 1.1. Food contribution to energy intake**

In 2002, the prevalence of overweight in Chinese adults was 22.8%, and the prevalence of obesity was 7.1%; it was estimated that the number of overweight and obese people had reached 200 million and over 60 million, respectively, in China. Because of the large proportion of overweight people, it can be predicted that the prevalence of obesity will increase significantly in the near future (1).

## Type 2 diabetes

Type 2 diabetes is a heterogeneous disorder. Clinical expression of the disorder requires both genetic and environmental factors. One theory concerning its etiology is that it is the result of the evolution of a thrifty genotype that had survival benefits in the past, but is detrimental in the current environment (3). An opposing theory is that it represents an adult metabolic response to fetal malnutrition (4).

Globally, the age-standardized prevalence of diabetes was 9.8% in men and 9.2% in women in 2008, leading to an estimated 173 million men and 173 million women with diabetes. The prevalence varies greatly worldwide (5-9); 40% of people with diabetes are from China and India, 10% from the USA and Russia, and 12% from Brazil, Pakistan, Indonesia, Japan, and Mexico (10).

Increasing trends of diabetes prevalence have been observed in both developed and developing countries (7) (9), (11). In 2002, the prevalence of diabetes among adults in China was 2.6%, and it was estimated that more than 20 million people in China had diabetes. There has been a rapid increase in diabetes prevalence in the Chinese population over the past decade (12-14). In 2010, the overall prevalence of diabetes was estimated to be 11.6% (95%CI, 11.3%–11.8%) in the Chinese adult population. The prevalence of type 2 diabetes among men was 12.1% (95%CI, 11.7%–12.5%) and among women 11.0% (95%CI, 10.7%–11.4%) (15).

Diabetes prevalence is strongly associated with age and is higher among urban residents than among rural populations in developing countries (9, 12, 13). In contrast, the prevalence of diabetes in developed countries decreases steadily as income or education level goes up (16-18).

The prevalence of type 2 diabetes and impaired fasting glucose (IFG) in Chinese adults was 2.6% and 1.9%, respectively, in 2002. The prevalence of diabetes increased with age and body mass index. Men and women had a similar prevalence of diabetes, but men had a significantly higher prevalence of IFG (2.2% for men and 1.8% for women). The prevalence of diabetes among the Chinese living in urban areas was twice to three times higher than its prevalence among those who lived in rural areas (4.5% for an urban adult and 1.8 for a rural adult), and the prevalence of IFG was one and a half times to twice higher (2.7% for urban and 1.6% for rural).

Hyperglycemia is associated with a cluster of metabolic abnormalities that include glucose intolerance, hypertension, dyslipidemia, a procoagulant state, and an increase in macrovascular disease (19). In 2002, the prevalence of hypertension, abnormal blood lipid levels, and metabolic syndrome among adults over 18 years old in China was 18.8%, 18.6%, and 6.6%, respectively. People living in urban areas had a higher prevalence of hypertension (19.3% vs. 18.6%), dyslipidemia (21.0% vs. 17.7%), and metabolic syndrome (5.4% vs 3.9%) (1).

## Risk factors for type 2 diabetes

It is clear that both genetic and environmental factors are important in the development of type 2 diabetes (19). In 2003, the joint WHO/FAO expert consultation report on diet, nutrition, and the prevention of chronic diseases summarized the strength of evidence of factors influencing type 2 diabetes (see **Table 1.1**) (20).

### *Convincing evidence*

<u>Obesity</u>

In all societies, overweight and obesity are associated with an increased risk of type 2 diabetes, especially when the excess adiposity is centrally distributed. In obese individuals, adipose tissue releases increased amounts of non-esterified fatty acids, glycerol, hormones, pro-inflammatory cytokines, and other factors involved in the development of insulin resistance (21).

**Table 1.1:** Summary of strength of evidence on lifestyle factors and risk of developing type 2 diabetes

| Evidence | Decreased risk | No relationship | Increased risk |
|---|---|---|---|
| **Convincing** | Voluntary weight loss in overweight and obese people<br>Physical activity | | Overweight and obesity<br>Abdominal obesity<br>Physical inactivity<br>Maternal diabetes[a] |
| **Probable** | Non-starch polysaccharides | | Saturated fats<br>Intrauterine growth retardation |
| **Possible** | n-3 fatty acids<br>Low glycemic index foods<br>Exclusive breast feeding[b] | | Total fat intake<br>Trans fatty acids |
| **Insufficient** | Vitamin E<br>Chromium<br>Magnesium<br>Moderate alcohol | | Excess alcohol |

[a] Includes gestational diabetes.
[b] As a global public health recommendation, infants should be exclusively breastfed for the first six months of life to achieve optimal growth, development, and health

Previous research indicates that people whose body fat is deposited more in the central or abdominal area, especially the intra-abdominal area, are at high risk of cardiovascular disease (22).

Several studies have found that the prevalence of type 2 diabetes increases with increasing BMI or waist circumference in different populations (23), (24, 25 ). As approximately 90% of people with type 2 diabetes are overweight or obese, obesity is seen as a significant contributory factor in its development (26). In the British population, mean BMI rose by 1.42 kg/m2 (95% CI 1.10–1.74) in 15 years; this was able to explain 26% (95% CI 17–38) of the type 2 diabetes increase (23).

In China, the prevalence of overweight has increased by 39% and the prevalence of obesity has increased by 97% in 10 years (1). The prevalence of diabetes among Chinese adults increased with increasing BMI, and the prevalence is 4.5 times higher in the participants with obesity class 3 (BMI ≥ 40 kg/m2) than in the participants with non-overweight/obesity. This is consistent with other Chinese population studies (27), (28).

Physical activity

There is convincing evidence that regular physical activity protects against unhealthy weight gain, whereas sedentary lifestyles, particularly sedentary occupations and inactive recreation such as watching television, promote weight gain (29).

Longitudinal studies have clearly indicated that greater physical activity reduces the risk of developing type 2 diabetes, regardless of the degree of adiposity (30-32). Vigorous exercise (i.e. training to an intensity of 80–90% of age-predicted maximum heart rate for at least 20 minutes, at least 5 times per week) has the potential to substantially enhance insulin sensitivity (33).

A 2006 study showed that, in China, only 8.0% of adults aged above 18 years engaged in regular exercise and 7.7% of people in occasional exercise (34). Among Chinese adults, traveling to and from work on foot or by bicycle seems to reduce the risk of overweight by 50% compared with taking the bus (35).

***Probable and possible evidence***

Fetal growth

The detrimental effects of poor fetal growth on the development of metabolic disease in later life have become clear (36-38). A recent meta-analysis of 30 studies found a significant graded association between low birth weight and increased risk of type 2 diabetes (39). Low birth weight has also been found to predict diabetes and the metabolic syndrome in Asian adults and children (37, 38, 40), thus lending support to the notion that fetal programming with exposure to poor nutrition in utero or during early childhood can promote a fat preserving or thrifty phenotype. These metabolic changes predispose individuals to insulin resistance and reduced beta cell function. Positive energy balance in later life, caused by rapid westernization of diet and lifestyle, may then exaggerate the accumulation of adiposity, particularly in the central depots (41).

Energy intake

A high total energy intake is the main driver of higher body weight in worldwide populations (42). Many dietary composition factors and dietary behaviors are associated with energy intake, and consequently associated with weight gain and obesity (43, 44). Experimental data convincingly show that people tend to eat a similar volume of food to feel satiated. Accordingly, consuming energy-dense foods could cause passive over-eating in terms of energy (45). Furthermore, energy-dense foods, usually high in fat and low in fiber, tend to be highly palatable and stimulate over-eating (46). It is believed that the generally accepted harmful impact of high fat diets on fat mass accumulation is primarily mediated by dietary energy density.

Fat intake

Obesity predisposes people to insulin resistance and is the most important determinant of type 2 diabetes (47, 48). Dietary fatty acids could affect insulin resistance independent of obesity. The effects of dietary fatty acids may be mediated through the fatty acid composition of cell membranes (49, 50). In fact, a high proportion of long-chain unsaturated fatty acids and a low proportion of saturated fatty acids in the phospholipids of the skeletal muscle membranes have been related to a high insulin sensitivity and seen to affect glucose-stimulated insulin secretion (50-52). In observational epidemiological studies, a high saturated fat intake has been associated with a higher risk of impaired glucose tolerance, and higher fasting glucose and insulin levels (52-55).

Carbohydrate intake

It has been reported that replacing fat with carbohydrate significantly elevates not only postprandial glucose levels but also postprandial and fasting insulin levels in patients with type 2 diabetes when the total energy intake is consistent (56).

The traditional Chinese diet is characterized by a high intake of plant-based foods, high in carbohydrates and very low in dietary fat. In 1982, 66% of energy intake came from carbohydrates, but the proportion has decreased significantly in the past 20 years (57). It has been reported that average BMI declines significantly ($p<0.05$) as the contribution of cereals to dietary energy increases. The relative risk of chronic diseases in the Chinese population was less when more than 55% of dietary energy came from cereals. When more than 75% of dietary energy intake derived from cereal foods, the relative risk of overweight and obesity, was reduced by 27%, but the risk of underweight increased by 24%. The study suggested that the optimum range of cereal energy intake to minimize disease was 55–65% (58).

The glycemic index (GI) is a quantitative measure of carbohydrate quality based on the blood glucose response after consumption (59). Glycemic load (GL) measures the entire blood glucose-raising potential of dietary carbohydrates and is calculated as the product of GI and total carbohydrates (60). Although the exact mechanisms by which high-GI diets may alter the risk of type 2 diabetes are unclear, two major pathways have been proposed (61, 62). First, the same amount of carbohydrate from high-GI foods, by definition, produces higher blood glucose concentrations and a greater insulin demand than do low-GI foods. It is possible that chronically increased insulin demand results in pancreatic exhaustion, which can result in glucose intolerance (62), Second, high-GI diets may directly increase insulin resistance. In animal studies, diets high in amylopectin or glucose produced more rapid and severe insulin resistance than did amylose-based diets (6, 63).

Dietary patterns

Dietary patterns, which reflect different combinations of food intake, have also been studied in relation to diabetes risk (64). Different methods have been used to study dietary patterns in epidemiological studies. First, principal components analysis is a frequently used exploratory approach to identify dietary pattern (65). Second, a hypothesis-oriented approach using predefined criteria to construct dietary pattern scores has been used (66). The reduced rank regression (RRR) method combines characteristics of the explanatory and hypothesis-oriented approaches to identify dietary pattern (67). Western dietary patterns, characterized by a high consumption of red meat, processed meat, high-fat food, sweets and deserts, have been examined and reveal a positive association with increased risk of developing type 2 diabetes in different populations (62, 68-70). Dietary patterns high in fiber, such as vegetables, fruit, whole grains, seeds and nuts, plus white meat sources like poultry could have protective effects against the incidence of type 2 diabetes (71). However, little work has been carried out to investigate Asian dietary patterns and, in particular, the Chinese diet. Three dietary patterns were identified in a study among 64,191 Chinese women. The result revealed that the ‘high dairy milk’ dietary pattern decreased diabetes incidence by almost 22%, in contrast to the ‘meat, fruit, and vegetable rich’ pattern, which increased the relative risk to 1.05 (72). A prospective cohort study among 690 Hong Kong Chinese showed that the ‘more vegetables, fruits, and fish’ pattern was associated with reduced risk and the ‘more meat and milk products’ pattern was associated with an increased risk of diabetes (73).

## Rationale and outline of the thesis

The traditional Chinese diet, characterized by a high intake of plant-based foods, high carbohydrate intake, and very low dietary fat, theoretically has cardio-protective potential. However, in tandem with China’s swift economic transition, this traditional dietary pattern is switching rapidly towards a more Western-style pattern. Several studies have shown that a Western dietary pattern may increase the risk of type 2 diabetes (62, 68, 69, 74-76). However, no national figures on the occurrence of type 2 diabetes, its determinants, and its relationship with dietary factors and lifestyle are currently available in China. National estimates of the prevalence of type 2 diabetes and IFG (Chapter 2) are needed to evaluate diabetes as a public health problem in China. Insight into diabetes determinants (Chapters 3–6) is necessary for the development of effective prevention strategies.

**Research questions**

The following research questions are addressed in this thesis:

1. What is the relationship between obesity and type 2 diabetes in China?
2. What is the relationship between dietary factors and type 2 diabetes in China?
3. What are the main Chinese dietary patterns, and what are their joint effects with physical activity on the likelihood of metabolic syndrome?
4. What is the relationship between fetal growth and type 2 diabetes in China?

**Description of the study**

The 2002 China National Nutrition and Health Survey (CNNHS) is a representative cross-sectional survey at national level, covering 31 provinces, autonomous regions, and the municipalities directly affiliated to the Central Government (Hong Kong, Macao, and Taiwan were not included). The multistage cluster sampling method was used for subject selection. Stage 1: all of China's 2,860 counties/districts/cities were divided into six areas (big cities, medium and small cities, rural 1, 2, 3, and 4) based on their type and the level of economic development (from high to low). Twenty-two counties/districts/cities from each area were randomly selected. A total of 132 counties/districts/cities were randomly selected at this stage. Stage 2: three townships/sub-districts were randomly selected from each selected county/district/city. A total of 396 townships/sub-districts were randomly selected at this Stage. Stage 3: two villages/neighborhood committees were randomly selected from the selected townships/sub-districts. A total of 792 villages/neighborhood committees were randomly selected at this stage. Stage 4: 90 households were randomly selected from each selected village/neighborhood, and finally, a total of 71,971 households were randomly selected to represent the national data.

The dietary survey was conducted among all members of 30 households randomly selected from the pre-selected 90 households. All family members above 2 years old in the selected households were invited to participate in the dietary intake assessment.

The information on food intake was collected using a 24-hour dietary recall method for three consecutive days (two weekdays and one weekend day) by trained interviewers.

The fasting body weight and height of participants were measured by trained investigators following the standardized procedure (77).

Fasting blood glucose levels were measured by trained technicians, and participants whose fasting glucose was 5.5mmol/l were given an oral glucose tolerance test (OGTT). To interpret the fasting and 2-h OGTT glucose levels, criteria from the World Health Organization Expert Committee on Diabetes Mellitus (1999 criteria) were used (78). Participants were classified as having diabetes (type 2), impaired glucose tolerance (IGT), or IFG. In the present study, the diagnosis glucose tolerance abnormality includes type 2 diabetes, IGT, and IFG.

To address the research questions, we analyzed data of 50,905 participants from the 2002 CNNHS. First, the prevalence of type 2 diabetes is described by reference to different populations, and the extent to which general and abdominal obesity currently account for the prevalence of the diagnosis glucose tolerance abnormality is examined (**Chapter 2**).

In **Chapter 3**, 20,210 individuals who completed dietary pattern data and underwent fasting blood sampling for the analysis of blood glucose were selected to investigate the association between dietary patterns and the presence of newly diagnosed glucose tolerance abnormalities in China. Dietary patterns had been established in previous studies by using factor analysis combined with cluster analysis of 56,442 men and women aged 18 years in the 2002 CNNHS(79).

In order to investigate whether the nutrition transition from high carbohydrate–low fat diet to the opposite increases the trend of diabetes, a ‘high fat/protein–low CHO score,’ an indicator of dietary pattern, was established. The participants were divided into quintiles of the high fat–low carbohydrate diet score. In **Chapter** 4, the odds of hyperglycemia and type 2 diabetes calculated per quintile is compared with that calculated in the lowest quintile. **Chapter 5** presents dietary patterns and their joint effects with physical activity on the likelihood of metabolic syndrome (MS) among 20,827 Chinese adults.

In order to address the research question about the notion that early developmental adaptations in response to under-nutrition may play an essential role in susceptibility to type 2 diabetes, particularly for those experiencing a ‘mismatched rich nutritional environment’ in later life, **Chapter 6** examines the associations of exposure to the Chinese famine (1959–1961) during fetal life and childhood with the risk of hyperglycemia and type 2 diabetes in adulthood.

This thesis ends with **Chapter 7**, in which the research findings are discussed in a broader context, and implications for future research and developments are explored.

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# CHAPTER 2

## Abdominal obesity and the prevalence of diabetes and intermediate hyperglycemia in Chinese adults

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## Abstract

**Objective**: To assess the association of indicators of general and abdominal obesity with the prevalence of type 2 diabetes (T2DM) and intermediate hyperglycaemia (IHG) in the Chinese population.

**Methods:** We used data of 50 905 adults aged 18–79 years in the 2002 China National Nutrition and Health Survey. Recommended Chinese cut-off values were used for BMI (24 kg/m2) and waist circumference (WC; 85 cm in men, 80 cm in women). Optimal cut-offs for waist:height ratio (WHtR) were determined from analyses of receiver-operating characteristic (ROC) curves.

**Results:** The prevalence of T2DM and IHG was 2.6% and 1.9% respectively. ROC curve analyses indicated 0.5 as the optimal cut-off value for WHtR in both sexes. High BMI, WC and WHtR were all associated with the prevalence of glucose tolerance abnormalities, with the highest prevalence ratio (PR) for high WHtR (men: PR=2.85, 95% CI 2.54, 3.21; women: PR=3.10, 95% CI 2.74, 3.51). When combining BMI and WHtR, in men either a high BMI or a high WHtR alone was associated with increased risk. Among women, a high BMI without a concomitant high WHtR was not associated with increased glucose tolerance abnormalities risk, whereas a high WHtR was associated with risk irrespective of BMI.

**Conclusions:** Among the Chinese adult population measures of central obesity are better predictors of glucose tolerance abnormalities prevalence than BMI. A WHtR cutoff point of 0.5 for both men and women can be considered as optimum for predicting (pre-) diabetes and may be a useful tool for screening and health education.

## Introduction

With the rapid development of the Chinese economy and society, lifestyle and dietary patterns have changed considerably during the past decades. There is now a double burden, posed by traditional health problems at one end of the spectrum, and escalating non-communicable diseases at the other. Recently the 2002 China Nutrition and Health Survey (CNHS) (1) showed that the prevalence of overweight in Chinese adults now amounts to 22.8%, and the prevalence of obesity to 7.1%. The estimated total number of overweight subjects in China is now about 200 million, and over 60 million Chinese subjects are obese.

Previously, the InterAsia study estimated the prevalence of diabetes in China to be 5.2%, or 12.7 million, men and 5.8%, or 13.3 million, women aged 35-74 years (2). Based on a an earlier survey in 1994, WHO estimated the number of diabetic subjects in China to be 21 million (3), or 2.4 % (4, 5). The most recent data are from CHNS 2002 and indicate that there currently are more than 20 million subjects with diabetes in China, and nearly another 20 million people with intermediate hyperglycemia or pre-diabetes (6).

As obesity is the main risk factor for T2DM, it is essential to assess the strength of the obesity-diabetes association in the Chinese population, also to provide an estimate of the proportion of diabetes that can be prevented by avoiding overweight and abdominal obesity. Anthropometric indexes such as the body mass index (BMI) and waist circumference (WC) remain the most commonly used tools for assessing body composition because of their simplicity and low cost, and provide sensitive methods for the estimation of total and central adiposity in groups (7).

In 1998, the WHO presented international definitions of overweight, body mass index (BMI) ≥ 25 $kg/m^2$, and central adiposity (waist circumference ≥94 cm for men, ≥80 cm for women) (8). As it is now well established that compared with Caucasians the Asian population accumulates fat mass at lower body weight (9), the Working Group on Obesity in China recommended the optimal range of healthy weight and appropriate cut-off points of BMI and WC specifically for Chinese adults. In these recommendations overweight is defined as a BMI ≥24 $kg/m^2$ and the suggested WC cut-offs are 85 cm for men and 80 cm for women (10).

Recently, several authors suggested to use the waist/height ratio (WHtR) as indicator of abdominal obesity, to be able to adjust for variations in body frame size (11). It was argued that the WHtR is not only more sensitive compared to BMI, but with a boundary value of 0.5 can be applied in all age groups, in men as well as women in different ethnic groups, thus circumventing the problem of group-specific waist cut-offs (11). In British adults the WHtR was a better indicator of cardiovascular and all cause mortality in comparison with BMI (12). In Japanese men and women WHtR was more strongly associated with cardiovascular risk factors and metabolic syndrome when compared to waist-hip ratio (13, 14).

To what extent general and abdominal obesity currently account for the prevalence of (pre-)diabetes in China needs to be established. The aim of the present study is therefore to assess the strength of the association of BMI, WC and WHtR with the prevalence of diabetes and pre-diabetes in the general Chinese population. Special attention is paid to the optimum predictive levels of WHtR in order to recommend cut-off values for diabetes prevention and health education in China.

## Subjects and Methods

*Sample design and study population*

For study sampling for the 2002 China National Nutrition and Health Survey the method of multi-steps cluster sampling was adopted (15). Finally, 71,971 households randomly selected to represent the national data. All family members above 2 years old were invited for the fasting blood glucose measurement, and finally data on fasting blood glucose are available on a total of 98,509 subjects (6).

We restricted the analyses to subjects aged 18-79 yr, including 51,970 men and women. We excluded 507 women who were pregnant or lactating. Also, a total of 558 subjects were excluded because of missing information on height, weight or WC measurement. Our final study population included 23,980 men and 26,925 women with complete information on fasting glucose and anthropometry.

*Anthropometric measurements*

Body weight was measured in the morning with a balance-beam scale while the subjects were wearing lightweight clothing and without shoes. Height was measured using a standard steel strip stadio-meter in bare footed subjects. Height was measured to the nearest 0.1 cm, and weight to the nearest 0.1 kg. BMI was calculated as weight (kg)/height (m)$^2$. Waist circumference (WC) was measured half way between costal border and the iliac crest at the end of exhalation. Waist to height ratio (WHtR) was calculated as WC (cm)/height (cm).

*Laboratory methods*

Fasting blood glucose levels were measured by trained technicians, and an oral glucose test (OGTT) was taken from subjects whose fasting glucose was greater or equal to 5.5 mmol/L. For interpretation of the fasting and 2-hr OGTT glucose levels criteria from the WHO Expert Committee on the Diabetes Mellitus (1999 criteria) (16) were used. Subjects were classified as diabetes (T2DM), impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). Prevalence rates of impaired fasting glucose or glucose tolerance, together referred to as intermediate hyperglycemia (IHG) (17), generally mirror those of diabetes. In numerous countries the prevalence of IHG has been shown to be higher than that of diabetes, confirming a potential for further rises in diabetes prevalence in the near future (18). We use the term glucose tolerance abnormality include to refer to the combined groups of subjects with T2DM, IGT and IFG.

*Quality control of anthropometric and blood measurements*

Body weight, height and waist circumference were all measured in the fasting state by trained investigators, and duplicate measurements in subgroups showed high reproducibility. Glucose was measured in plasma, with heparin lithium added to tube to avoid glycolysis by red blood cells. All fasting glucose samples were measured within 4 hours of blood sampling. Every tenth sample was measured twice (correlation coefficients of duplicate measurements was 0.98), at the same time, one reference sample, one quality control sample and one blind sample were measured before every 30th samples.

*Statistical analyses*

Data were expressed as mean±SD or percentage. Statistical analyses were performed separately for men and women. Characteristics of the study subjects according to diabetes status were compared by Student's t-test and $\chi 2$ test for continuous and categorical variables, respectively.

Receiver operating characteristic (ROC) analysis was performed to determine cut-off values to minimize the total number of misclassifications and evaluate the general performance of BMI, WC and WHtR in diagnosing glucose tolerance abnormality. An index reflecting the overall accuracy of the diagnostic test derived from an ROC analysis is the area under the curve (AUC). The area under the ROC curve can take values between 0 and 1, where 1 is a perfect screening test and 0.5 is a test equal to chance. The distance in the ROC curves were calculated according to the equation square root of $[(1 - \text{sensitivity})^2 + (1- \text{specificity})^2]$ (19). Youden's Index was calculated according to the equation sensitivity+specificity-1. The optimal cut-off value for WHtR was based on the shortest distance and the highest value of the Youden's index.

Glucose tolerance abnormality prevalence rates according to different categories of BMI, WC and WHtR were analyzed by $\chi 2$- test. As indicated by Spiegelman and Hertzmark adjusted prevalence ratio's can now easily be calculated using log-binomial regression models in SAS (20). This is useful as at higher disease prevalence rates, the OR tends to overestimate of the PR (21, 22).

Adjusted prevalence ratios (PR) and their 95% confidence intervals were calculated by using the SAS PROC GENMOD procedure (20). We adjusted for any potentially confounding effects of these lifestyle or socioeconomic factors in the log-binomial regression models. All analyses were conducted with the use of SAS software (version 9.1; SAS Institute Inc, Cary, NC).

## Results

Characteristic of the study population are presented in **Table 2.1**. Persons who lived in the urban areas were on average older, more highly educated, less likely to be smokers (in men), and had higher mean BMI, WC and WHtR.

**Table2.1** Characteristics of the study population by age, sex and area, 2002 China National Nutrition and Health Survey

| | Urban | | Rural | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| N | 8320 | 9794 | 15660 | 17131 |
| Age (year)(mean±SD) | 48.0±15.2* | 47.0±14.5* | 44.6±14.1 | 44.0±13.5 |
| Education (year) (mean±SD) | 10.4±3.5* | 9.2±4.1* | 8.1±3.3 | 6.3±3.9 |
| Smoker (%) | 50.4* | 3.9 | 57.3 | 2.9 |
| BMI (kg/m$^2$) (mean±SD) | 24.1±3.6 | 24.0±3.8 | 22.5±3.2 | 23.0±3.6 |
| WC (cm) (mean±SD) | 84.3±10.5* | 78.4±10.3* | 78.0±9.8 | 75.4±9.9 |
| WHtR(mean±SD) | 0.50±0.06* | 0.50±0.07* | 0.47±0.06 | 0.49±0.06 |

* P<0.0001, compared to Rural area in same sex

**Table 2.2** Prevalence of diabetes (T2DM) and impaired glucose regulation (IHG) in Chinese adults (2002 China National Nutrition and Health Survey)

| | Age | Urban | | | Rural | | | National[b] | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | group | Men | Women | M+W[a] | Men | Women | M+W[a] | Men | Women | M+W[a] |
| T2DM | Total[c] | 4.53 | 4.32 | 4.45 | 1.70 | 1.97 | 1.83 | 2.54 | 2.66 | 2.60 |
| | 18~44 | 2.30 | 1.67 | 1.95 | 1.12 | 0.86 | 0.98 | 1.48 | 1.10 | 1.27 |
| | 45~59 | 8.20 | 7.44 | 7.78 | 2.33 | 3.55 | 2.96 | 3.93 | 4.63 | 4.29 |
| | 60~ | 13.28 | 12.92 | 13.13 | 3.94 | 4.88 | 4.41 | 6.47 | 7.06 | 6.77 |
| IHG | Total[c] | 2.97 | 2.53 | 2.70 | 1.89 | 1.45 | 1.56 | 2.21 | 1.77 | 1.90 |
| | 18~44 | 2.12 | 1.01 | 1.50 | 1.49 | 0.85 | 1.14 | 1.68 | 0.90 | 1.25 |
| | 45~59 | 3.59 | 2.78 | 3.15 | 2.51 | 2.30 | 2.39 | 2.80 | 2.43 | 2.60 |
| | 60~ | 4.00 | 4.87 | 4.43 | 3.13 | 2.97 | 3.05 | 3.37 | 3.49 | 3.42 |

a Adjusted for sex
b Adjusted for area (Urban/Rural)
c Adjusted for age

The prevalence of T2DM (either newly diagnosed using fasting and post-load glucose levels or treated) and IHG increased with age, and was higher in urban than in rural areas. The overall prevalence of T2DM amounted to 2.6%, and IHG was present in 1.9% of the subjects (**Table 2.2**).

As expected BMI, WHtR and WC were all significantly inter-correlated in both sexes (BMI vs. WC, men r=0.86 ; women r=0.84; BMI vs. WHtR, men r=0.86, women r=0.82; WC vs. WHtR men r=0.95, women r=0.96; all p values<0.0001). For the diagnosis glucose tolerance abnormality the AUCs of the ROC curves ranged from 0.70 to 0.75 (**Table 2.3**). In general, the AUC for BMI was lower than for WC or WHtR. The AUCs of WC and WHtR were higher in women than in men.

**Table 2.3** Associations between BMI and waist indices and prevalence of glucose tolerance abnormalities, analysed by area under the receiver operating characteristic (ROC) curves (AUC), prevalence ratio's (PR) and population attributable risks (PAR), 2002 China National Nutrition and Health Survey

| Indicator | | AUC | SE | 95% CI | Adjusted PR┼ | 95%CI | PAR┼┼(%) |
|---|---|---|---|---|---|---|---|
| BMI | Men | 0.705 | 0.007 | 0.692- 0.719 | 1.607* | 1.535-1.682 | 44.2 |
| | Women | 0.700 | 0.007 | 0.687- 0.713 | 1.546* | 1.482-1.613 | 49.3 |
| WC | Men | 0.730 | 0.007 | 0.717- 0.743 | 1.677* | 1.600-1.757 | 56.1 |
| | Women | 0.754 | 0.006 | 0.742- 0.766 | 1.733* | 1.658-1.811 | 58.1 |
| WHtR | Men | 0.737 | 0.006 | 0.724- 0.749 | 1.675* | 1.598-1.756 | 56.2 |
| | Women | 0.753 | 0.006 | 0.741- 0.765 | 1.679* | 1.606-1.756 | 56.9 |

┼prevalence ratio per 1 SD increased ,adjusted by area, education years, smoking and age, * P<0.0001
┼┼Population attributable risk comparing in fifth to first quintile categories

Expressed per 1 SD the adjusted PRs were higher for WHtR and WC then BMI in both men and women (Table 2.3). We also compared the Population attributable risk (PAR) comparing the highest versus the lowest quintile of each index. The PAR for the highest BMI quintile was 44% for men and 49% for women. For WC and WHtR PARs were observed, about 56% for men and 57-58% for women.

Because there are no generally accepted reference values to define abdominal obesity by WHtR, the influence of different WHtR cut-offs on the test characteristics was investigated (**Table 2.4**). WHtR thresholds of 0.50 in men and 0.52 in women had the largest AUC and the shortest distance in the ROC curve. The highest Youden's Index was found for the cut-off value 0.50 in both men and women.

Regardless of the cut-off points used, BMI, WC and WHtR, were all significantly associated with the prevalence of glucose tolerance abnormality in both sexes (**Table 2.5**). In women the PRs were higher for WC and WHtR than for BMI. For men this difference between obesity indices was less clear. The highest prevalence ratio was observed for WHtR ≥0.5 in both men and women.

**Table 2.4** Test characteristics of WHtR predicting prevalence of glucose tolerance abnormalities, 2002 China National Nutrition and Health Survey

| | WHtR | Sensitivity (%) | Specificity (%) | AUC | 95% CI | Distance in ROC curve | Youden's Index |
|---|---|---|---|---|---|---|---|
| Men | 0.48 | 55.7 | 80.2 | 0.682 | 0.669-0.694 | 0.485 | 0.359 |
| | 0.50 | 66.3 | 70.1 | 0.692 | 0.678-0.706 | 0.451 | 0.364 |
| | 0.52 | 75.7 | 58.3 | 0.682 | 0.667-0.697 | 0.483 | 0.340 |
| | 0.54 | 83.7 | 43.8 | 0.653 | 0.637-0.670 | 0.585 | 0.275 |
| Women | 0.48 | 48.8 | 85.9 | 0.669 | 0.658-0.681 | 0.531 | 0.347 |
| | 0.50 | 60.7 | 78.4 | 0.699 | 0.687-0.711 | 0.448 | 0.391 |
| | 0.52 | 71.0 | 67.8 | 0.705 | 0.692-0.719 | 0.433 | 0.388 |
| | 0.54 | 79.1 | 56.3 | 0.691 | 0.676-0.705 | 0.484 | 0.354 |

Adjusted PRs were highest with both a higher BMI and WHtR in either sex, suggesting that measurement of both parameters could much improve the predictive power **(Table 2.6)**. However, high BMI without concomitant high WHtR was not associated with increased prevalence of glucose tolerance abnormality in women, whereas in men both high BMI and high WHtR alone were associated with a moderate increased risk.

## Discussion

The proportion of men and women with type 2 diabetes and obesity have increased throughout Asia (23), and this nationwide survey shows that the prevalence of Type 2 diabetes in China is 2.6%, and 1.9% for IHG. Since historical, nationally representative prevalence data of China are not available, we cannot describe the exact trends of diabetes among the Chinese. Comparing the prevalence of Type 2 diabetes between the urban and rural residents however, we found that urban residents have a more than two times higher prevalence than rural residents, as reported in other Chinese studies as well (2, 24, 25). This suggests that the rate of diabetes will increase in rural communities as they become urbanized.

Data from cohort studies in Western countries have shown that BMI is strongly associated with increased risk of developing diabetes(26, 27) and such association has also been shown in other ethnic groups, including a cohort of Chinese women (28). In the present study we used overweight and obesity cut-off points of BMI as recommended by the WHO and by the China Obesity Working Group. Our results show that BMI is an independent predictor of diabetes after adjustment by age, area, years of education, smoking and physical activity. Diabetes was three-fold more prevalent in those with a BMI of 24 $kg/m^2$ or more.

Abdominal obesity, as indicated by waist circumference or waist-hip ratio, is generally more closely correlated to diabetes or glucose levels than general obesity itself in various population groups (27-32). In this large Chinese study sample the AUC of ROC curve for waist circumference is larger than for BMI in both sexes, and the adjusted prevalence of (pre)diabetes is three times higher in men and women with a waist above the Chinese recommended cut-off values than in those with smaller waist. This confirms the importance of abdominal obesity in the general Chinese population.

However, although waist circumference is closely related with CHD, diabetes or its risk factors, the limits to be used for screening or health education vary across the sexes and ethnic origin. The WHtR, waist-to-height ratio, has therefore been proposed (33). In British adults, the WHtR was a better indicator of cardiovascular and all cause mortality in comparison with BMI (12). In Japanese men and women (13, 14), WHtR was more strongly associated with cardiovascular risk factors and metabolic syndrome when compared to waist/hip ratio. Compared to WC and the waist/hip ratio, WHtR appeared to be a better diabetes predictor in a follow-up of adult men from Teheran (34). In a previous study in middle aged Hong Kong Chinese subjects, this ratio was associated with the risk of diabetes mellitus, but was not superior to WC alone (35).

Whether WHtR could be an effective predictor of diabetes has not been evaluated in the general Chinese population before. Our ROC analysis revealed that among men the AUC was highest for the WHtR, while for women this was as high as for WC. Comparing the adjusted prevalence ratios using various cut-off points in men and women separately, the highest risk ratios were observed for the 0.5 cut-off in both men and women, also in comparison with BMI and WC. Thus, WHtR is a good predictor of glucose tolerance abnormalities among Chinese adults, and a boundary value of 0.5, as proposed (11, 36), seems a good choice for both men and women. One of the advantages of the WHtR above WC is the potential to use an overall cut-off value, possibly also in children (37, 38).

We also examined whether combining BMI and WHtR could improve the predictive power. Interestingly, a high BMI without concomitant high WHtR was not associated with increased diabetes prevalence among women. This enforces the importance of the use of an indicator of abdominal obesity rather than body weight for predicting diabetes in Chinese women. For men, the impact of BMI and WHtR appeared to be synergistic, with the highest risk observed for the combined presence of high BMI and high WHtR.

The population attributable risks for women ranged from 49% for high BMI to 57% for high WHtR. Among men the population attributable risk was around 44% for high BMI and 56% for high WHtR. Thus about 56% of the prevalence of glucose tolerance abnormalities in the whole Chinese adult population may be preventable if central obesity was eliminated. Although the diabetes rates are still relatively low, this indicates the potential of improvement in the treatment and prevention of obesity in China for the health care burden.

In summary, our results indicate that among the Chinese adult population measures of central obesity are better predictors of prevalence of glucose tolerance abnormalities than measures of overall obesity, especially among women. A cut-off value of WHtR ≥0.5 for both men and women can be considered as optimum values for a reduced risk of glucose tolerance abnormalities, and may be a useful tool in screening and health education.

**Table 2.5** Adjusted prevalence ratios (PR) for different cut-off points of obesity indices according to sex, 2002 China National Nutrition and Health Survey

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | N | Glucose tolerance abnormalities (%) | Adjusted PR(95% CI)┼ | N | Glucose tolerance abnormalities (%) | Adjusted PR(95% CI)┼ |
| BMI(kg/$m^2$) | | | | | | |
| ≥24 vs <24[1] | 8541 vs15439 | 11.5 vs3.1* | 2.780 (2.482~3.115)* | 10398 vs16527 | 10.4 vs3.3* | 2.268 (2.041~2.519)* |
| ≥25 vs <25[2] | 6421 vs17559 | 12.5 vs3.8* | 2.480 (2.229~2.759)* | 7905 vs19016 | 11.6 vs3.7* | 2.195 (1.986~2.426)* |
| ≥28 vs <28[1] | 2057 vs21923 | 14.9 vs5.3* | 2.153 (1.894~2.446)* | 2986 vs23939 | 14.9 vs4.9* | 2.146 (1.921~2.397)* |
| ≥30 vs <30[2] | 745 vs23235 | 16.6 vs5.8* | 2.247 (1.867~2.704)* | 1318 vs25607 | 18.2 vs5.4* | 2.356 (2.051~2.705)* |
| WC(cm) | | | | | | |
| ≥80 vs<80[1] | | | | 9221 vs17704 | 12.6 vs2.6* | 3.097 (2.769~3.465)* |
| ≥85 vs<85[1] | 7610 vs16370 | 12.3 vs3.2* | 2.703 (2.415~3.025)* | | | |
| WHtR | | | | | | |
| ≥0.50 vs <0.50 | 8610 vs 15370 | 11.9vs 2.8* | 2.851 (2.535~3.207)* | 11229 vs 15696 | 11.4 vs 2.2** | 3.103 (2.741~3.513)* |

┼Adjusted by area, education years, smoking and age
[1]Cut-offs for overweight and obesity recommended by the Working group on Obesity in China (10)
[2]Cut-offs for overweight and obesity as recommended by WHO (8)
*P<0.0001 comparing the prevalence of T2DM and IHG between the groups under and over cut-off point

**Table 2.6** Adjusted prevalence ratios (PR) for glucose tolerance abnormalities for BMI combined WHtR according to sex, 2002 China National Nutrition and Health Survey

| | Men | | | Women | | |
|---|---|---|---|---|---|---|
| | N | Glucose tolerance abnormalities (%) | Adjusted PR(95% CI)┼ | N | Glucose tolerance abnormalities (%) | Adjusted PR(95% CI)┼ |
| BMI & WHtR | | | | | | |
| <24 and <0.5 | 13859 | 2.5 | 1.000 | 13811 | 2.2 | 1.000 |
| <24 and ≥0.5 | 1580 | 8.2 | 2.002 (1.622~2.470)* | 2761 | 9.0 | 2.339 (1.945~2.814)* |
| ≥24 and <0.5` | 1511 | 5.8 | 2.184 (1.722~2.769)* | 1885 | 2.7 | 1.186 (0.879~1.599) |
| ≥24 and ≥0.5 | 7030 | 12.8 | 3.481 (3.054~3.968)* | 8513 | 12.1 | 3.429 (2.999~3.921)* |

┼Adjusted by area, education years, smoking and age
*P<0.001

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# CHAPTER 3

## Dietary patterns and glucose tolerance abnormalities in Chinese adults

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## Abstract

**Objective:** To investigate the association of the dietary pattern with the presence of newly diagnosed glucose tolerance abnormalities among Chinese adults.

**Research Design and Methods:** A total of 20,210 adults aged 45-69 years from the 2002 China National Nutrition and Health Survey were included. Information on dietary intake was collected using a validated food frequency questionnaire. Factor analysis and cluster analysis were used to identify the food factors and dietary pattern clusters.

**Results:** Four dietary pattern clusters were identified ('Green Water', 'Yellow Earth', 'Western Adopter', and 'New Affluence'). The prevalence of glucose tolerance abnormalities ranged from 3.9% in the Green Water to 8.0% in the New Affluence. After adjustment for area, age, sex, current smoking and physical activity, subjects in the Yellow Earth cluster (prevalence ratio 1.22 [95%CI 1.04-1.43]) and New Affluence cluster (2.05 [1.76-2.37]) had significantly higher prevalence rates compared with those for the Green Water cluster. After further adjustment for BMI and waist-to-height ratio, the elevated risk in the New Affluence remained statistically significant.

**Conclusions:** Dietary patterns and food factors are associated with the presence of glucose tolerance abnormalities in China, even independent of obesity. A New Affluence diet is an important modifiable risk factor, which needs attention from the prevention point of view.

## Introduction

The prevalence of type 2 diabetes is increasing rapidly worldwide (1). The 2002 China National Nutrition and Health Survey showed that 2.6% of Chinese adults have diabetes, translating to >20 million people (2). Behavior and lifestyle factors, such as eating habits and physical activity, are recognized as playing an important role in the development of diabetes. The traditional approach to investigate diet-disease associations focuses on single dietary components, such as single nutrients or foods (3-8). However, individuals eat meals instead of foods or nutrients, making it more difficult to separate the effect of individual dietary components. The effect of the overall diet can be studied with dietary pattern analyses. This approach is used increasingly in studies on the relationship between diet and diabetes among Western populations. Some studies suggest that the adoption of a western dietary pattern, characterized by red meat, processed meat, French fries, high-fat dairy products, refined grains, sweets, and desserts, may be associated with increased incidence of type 2 diabetes (9-12).

Little work, however, has been done to investigate Asian dietary patterns and, in particular, the Chinese diet. Recently four Chinese dietary patterns were identified in a study on dietary habits and obesity among Chinese adults (13). The dietary patterns identified were considered to be highly realistic within the nutrition transition framework in China. In the present study, we used these four dietary patterns to investigate the association with the presence of newly diagnosed glucose tolerance abnormalities in China.

## Research Design and Methods

The 2002 China National Nutrition and Health Survey is a national representative cross-sectional study on diet and chronic disease. It covered all 31 provinces, autonomous regions, and municipalities directly under the central government throughout China (except Taiwan, Hong Kong, and Macao). Participants were recruited by use of a stratified multistage cluster sampling design. The country was divided into six strata: large cities, small to medium cities, class 1 rural areas, class 2 rural areas, class 3 rural areas, and class 4 rural areas, according to their economic characteristics and social development. The first stage of sampling involved the random selection of 22 districts (urban) or counties (rural) from each of the six strata. The second stage involved the random selection of three neighborhoods (urban) or townships (rural) from each of the selected districts/counties. From each of the neighborhoods or townships, two residential committees (urban) or villages (rural) were randomly selected; 90 households were randomly sampled from each village. A total of 795 residential committees or villages and 68,828 families were sampled. About one-third of households were selected to participate in the dietary survey. All participants aged ≥15 years completed an interview with a structured food frequency questionnaire. All family members of these dietary survey participants, who were aged>2 years, were invited for the measurement of fasting blood glucose. An oral glucose tolerance test (OGTT) was undertaken in subjects whose fasting glucose was ≥5.5 mmol/l.

Once the village/neighbourhood committee decided to participate, the individual response rate was always >90%. Of the 68,925 subjects who attended the dietary survey, 60,158 participated in the fasting glucose measurement, a response rate of 87%. Among the 5,887 subjects whose fasting glucose level was >5.5 mmol/l and who should therefore have participated in the OGTT, 1,818 subjects did (response rate 31%). Among the subjects who finalized the food frequency questionnaire, 6% were excluded because of extreme values, including daily energy intake >5,000 kcal. Further details on this survey have been published elsewhere (2).

For the present study, we used data of 20,866 subjects aged 45-69 years who had a completed a food frequency questionnaire and underwent fasting blood sampling for analysis of blood glucose. All subjects who were known to have diabetes before the survey were excluded from the analyses (n=656), because they may have changed their dietary habits. The final study population comprised 20,210 individuals.

*Dietary Assessment*

A validated semi-quantitative food frequency questionnaire was used to investigate the usual diet in the previous 1 year before the study (14). A previous article described the construction of dietary patterns by using factor analysis combined with cluster analysis in 56,442 men and women aged >18 years in the 2002 China National Nutrition and Health Survey for whom dietary data were complete (13). In short, four factors were identified by applying the principal components method with oblique rotation based on the quartiles of the consumption quantity (online Appendix 1, available at http://care.diabetesjournals.org/ cgi/content/full/dc09- 0714/DC1).

Subsequently, we used the factor scores in cluster analysis with a two-step approach. First, hierarchical cluster analysis by randomly filtering 1% of the total number of participants was used to help identify the number of clusters and to determine the initial cluster centers for the subsequent K-means cluster analysis. A plot of the agglomeration coefficients in the successive steps revealed an elbow at the four-cluster solution. We then saved the means of the four clusters as initial cluster centers for the K-means cluster. By using the output from the hierarchical clustering, K-means cluster method was used to calibrate the solution for all cases. In the end, all cases were assigned to each of the four clusters (Appendix 1,2). We calculated the average food consumption of different diet patterns as the average amount (grams) per reference men per day, a men being an 18-year-old man with light physical activity level, whose reference energy intake is 2,400 kcal. Mean values of individual amounts in reference men among each group were then calculated. According to these characteristic of food intake, the four dietary patterns were labeled as ‘Green Water’ (like the rice area in the Southeast), ‘Yellow Earth’ (their food is mainly produced on the dry and hilly land, like the mountain area in the Northwest), ‘New affluence’ (mainly well-to-do individuals) and ‘Western adopter’ (mainly young people, a more Western-oriented food style), respectively.

*Ascertainment of glucose tolerance abnormality*

Fasting blood glucose level were measured by trained technicians, and an OGTT was taken from subjects whose fasting glucose was ≥ 5.5 mmol/L. For interpretation of the fasting and 2-h OGTT glucose levels, criteria from the World Health Organization Expert Committee on the Diabetes Mellitus (1999 criteria) were used. Subjects were classified as diabetes (T2DM), impaired glucose tolerance (IGT), or impaired fasting glucose (IFG). In the present study, the diagnosis glucose tolerance abnormality includes Type 2 diabetes, IGT, and IFG.

*Measurement of behavioural factors*

Information on current smoking and drinking was collected by trained investigators from face-to-face interviews. Current smoking was identified as having smoked at least one piece a week in the past 30 days, and alcohol drinking was identified as drinking alcohol at least once per week.

BMI (weight in kilograms divided by the square of height in meters) was calculated from direct measurements of fasting body weight and height. Our recent study (15) showed that the waist-to-height ratio (WHtR) was more strongly associated with (pre-)diabetes than waist circumference in Chinese adults, so we used WHtR as an indicator of abdominal obesity. Physical activity was recorded as three-level variable (light, moderate and heavy), as recommended by the China Nutrition Society (16), to reflect total energy expenditure.

*Statistical methods*

Factor analysis and cluster analysis were performed by using the SPSS statistical system (version 13.0; SPSS, Chicago, IL). Subjects' characteristics were compared between the dietary clusters using the $\chi 2$ statistic for discrete variables and ANOVA for continuous variables. The age-adjusted and multiple adjusted prevalence ratios and their 95% CIs of glucose tolerance abnormality between different dietary clusters and different food factors were calculated after adjustment for age, family history of diabetes, smoking status, WHtR and physical activity level using the Cox regression analysis PHREG Procedure in SAS (version 9.1; SAS Institute, Cary, NC), in which survival time is artificially set equal to 1(17).

## Results

*Subjects characteristics*

As shown in **Table 3.1** and **3.2**, the Green Water cluster was characterized by living in rural areas, having higher physical activity, being more likely to smoke and drink alcohol, but being less frequently overweight and obese, and having a higher consumption of rice and vegetables and a moderate intake of animal foods. The Yellow earth cluster was characterized by higher consumption of wheat flour, tubers, other cereals and lower consumption of vegetables, fruit and animal food. The New affluence cluster was characterized by living in urban areas, being less physical active, having more smokers, alcohol users, and overweight individuals, and having a higher intake of animal foods and soybean products. The Western adaptor diet was characterized by a high consumption of animal food, cakes and drinks.

*Dietary pattern and glucose tolerance abnormality*

The prevalence of glucose tolerance abnormality was significantly different among subjects with different dietary patterns. Subjects of the Green Water cluster had the lowest prevalence of glucose tolerance abnormality (3.9%), whereas the highest prevalence was found in the New Affluence pattern (8.0%) **(Table 3.1).**

After adjustment for area, age, sex, smoking, alcohol drinking, physical activity level, and family history of diabetes, the association between diet clusters and glucose tolerance abnormalities was attenuated but remained significant for the New Affluence (prevalence ratio 1.45 [95% CI 1.21-1.72] and Yellow Earth (1.26 [1.07-1.48]) clusters. The association disappeared after further adjustment for BMI or WHtR in the Yellow Earth cluster but remained significant in the New Affluence cluster (**Table 3.3**).

**Table 3.1** Selected characteristics of Chinese adults according to dietary cluster (2002 China National Nutrition and Health Survey)

| | | Green Water | Yellow Earth | New Affluence | Western Adopter |
|---|---|---|---|---|---|
| N (%) | | 7314(36.2) | 5651(28.0) | 4923 (24.4) | 2322 (11.5) |
| Sex (% men) | | 49.6 | 45.2* | 46.5* | 50.3 |
| Age (%) | 45~59 yrs | 74.3 | 72.0* | 69.1* | 75.1 |
| | 60~69 yrs | 25.7 | 28.0 | 30.9 | 24.9 |
| Area (%) | Urban | 24.1 | 15.9* | 64.2* | 65.4* |
| | Rural | 75.9 | 84.1 | 35.8 | 34.6 |
| Current smoker (%) | | 32.6 | 28.6* | 27.8* | 30.3* |
| Alcohol drinker (%) | | 28.7 | 16.5* | 22.8* | 29.0 |
| BMI(%) | <18.5 $kg/m^2$ | 8.9 | 5.2* | 2.6* | 3.2* |
| | 18.5-23.9 | 61.8 | 53.3 | 40.3 | 44.4 |
| | 24-27.9 $kg/m^2$ | 22.9 | 29.7 | 39.8 | 37.5 |
| | ≥28 $kg/m^2$ | 6.4 | 11.8 | 17.3 | 14.9 |
| WHtR>0.5(%) | | 37.1 | 45.6* | 59.9* | 55.8* |
| Physical activity level (%) | | 33.9 | 32.5* | 71.5* | 72.6* |
| | | 17.7 | 20.5 | 12.2 | 15.9 |
| | | 48.4 | 47.0 | 16.3 | 11.5 |
| Annual family income per | | | | | |
| <2000 RMB | | 45.9 | 65.7* | 25.0* | 16.2* |
| 2000-4999 RMB | | 34.1 | 24.5 | 27.2 | 26.3 |
| ≥5000 RMB | | 20.0 | 9.8 | 47.8 | 57.5 |
| Education level(%) | | | | | |
| Illiterate | | 21.3 | 23.1* | 8.2* | 6.9* |
| Primary school | | 45.9 | 41.0 | 27.1 | 26.5 |
| High school | | 31.1 | 34.7 | 55.9 | 55.8 |
| Above High school | | 1.7 | 1.2 | 8.8 | 10.8 |
| Glucose tolerance | | 285(3.9) | 271(4.8)* | 394(8.0)* | 146(6.3)* |
| Diabetes | | 148(2.0) | 123(2.2) | 213(4.3)* | 80(3.5)* |
| IFG | | 107(1.5) | 114(2.0)* | 134(2.7)* | 54(2.3)* |
| IGT | | 55(0.8) | 56(1.0) | 77(1.6) | 24(1.0) |

Data are n (%) or %. *Significantly different from Green Water pattern (Pearson's $\chi^2$ test), p<0.05.

**Table3. 2** Dietary intake of Chinese adults according to dietary cluster (2002 China National Nutrition and Health Survey)

| | Green Water | Yellow Earth | New Affluence | Western Adopter |
|---|---|---|---|---|
| Rice and rice products | 399.6±157.7 | 91.0±115.5* | 156.4±118.3* | 233.1±144.7* |
| Wheat and products | 26.4±51.1 | 264.9±183.3* | 170.5±165.1* | 99.1±122.2* |
| Other cereals | 4.6±28.2 | 59.8±85.8* | 27.3±54.3* | 16.9±34.9* |
| Starchy Tubers | 18.3±41.4 | 70.8±104.9* | 42.0±68.2* | 30.5±48.9 * |
| Pork | 47.8±55.8 | 16.1±33.8* | 52.4±60.5* | 64.7±65.7* |
| Beef/lamb | 2.1±8.7 | 2.9±19.5* | 14.2±35.3* | 12.5±35.9* |
| Poultry | 8.0±24.6 | 1.4±8.8* | 12.9±35.1* | 16.1±27.3* |
| Fish and Shrimps | 23.7±45.7 | 3.3±14.5* | 27.7±48.9* | 35.5±47.6* |
| Eggs | 19.6±24.4 | 29.2±34.1* | 47.0±38.5* | 39.3±33.2* |
| Dairy products | 6.6±44.9 | 15.1±74.4* | 104.8±168.6* | 98.1±159.0* |
| Soybean products | 9.9±14.0 | 7.2±10.3* | 14.7±16.8* | 14.4±13.5* |
| Dry beans | 5.1±30.8 | 6.4±35.1* | 10.0±44.5* | 11.9±39.4 * |
| Vegetables | 309.0±175.6 | 184.9±155.9* | 248.7±160.5* | 273.1±161.4* |
| Dry vegetables | 3.3±21.7 | 3.3±22.6* | 5.0±33.4* | 4.5±26.0* |
| Cake | 3.4±16.3 | 2.2±10.2* | 12.6±28.7* | 18.7±30.4* |
| Fruit | 43.1±63.8 | 50.6±73.1* | 113.0±101.1* | 114.6±98.6 * |
| Nuts | 3.0±14.4 | 2.5±12.2 | 8.5±22.4* | 12.5±25.6* |
| Low-degree alcohol | 11.9±63.3 | 5.2±71.8* | 5.8±30.6 * | 8.5±38.9* |
| High-degree alcohol | 14.5±182.0 | 5.4±29.6* | 10.7±83.9 | 8.3 ±35.0 |
| Beer | 28.2±317.0 | 7.1±60.0* | 25.4±177.2 | 67.0±596.1* |
| Wine | 0.7±29.2 | 0.2±7.2 | 0.8±13.3 | 6.2±207.6 |
| Juice | 2.5±19.2 | 1.4±16.0* | 4.4±29.1* | 32.9±66.7* |
| Other Beverages | 9.2±65.6 | 3.6±53.7* | 23.3±143.2 * | 38.7±117.5* |
| Vegetable oil | 30.0±31.0 | 34.0±34.4* | 39.9±31.6* | 38.2±30.4* |
| Animal fat | 13.4±24.2 | 6.9±19.9* | 3.7±13.2* | 4.1±13.5* |

Data are means±SD grams per day. *Mean is significantly different from the Green Water Pattern (ANOVA) ,P<0.05

**Table 3.3** Prevalence ratios (95% CI) of glucose tolerance abnormality according to dietary cluster (2002 China National Nutrition and Health Survey)

| | Green Water | Yellow Earth | New Affluence | Western Adopter |
|---|---|---|---|---|
| Model 1 | 1.0(reference) | 1.22 (1.04,1.43)* | 2.05 (1.76,2.37)** | 1.60 (1.32,1.95) ** |
| Model 2 | 1 | 1.26 (1.07,1.48)* | 1.45 (1.21,1.72)** | 1.07 (0.84,1.36) |
| Model 3 | 1 | 1.04 (0.88,1.22) | 1.19 (1.01,1.41) * | 0.95 (0.76,1.19) |
| Model 4 | 1 | 1.12 (0.93,1.35) | 1.24 (1.04,1.49) * | 0.99 (0.78,1.26) |

Model 1: unadjusted

Model 2: adjusted for area (urban/rural), age, sex, current smoking, physical activity level, family history of diabetes, education level and family income

Model 3: additionally adjusted for BMI

Model 4: Model 2 additionally adjusted for WHtR

* $p<0.05$, ** $p<0.0001$.

## Conclusions

Currently, China is undergoing a remarkably fast shift towards a stage of nutrition transition dominated by a high intake of fat and animal foods, as well as a high prevalence of diet-related chronic diseases， such as obesity, diabetes and cardiovascular disease (2, 18). The four dietary patterns identified reflect the main dietary characteristics of the Chinese population under nutrition transition. In addition, we found that these dietary patterns are associated with the presence of glucose tolerance abnormalities. The Green Water pattern, characteristically high in rice and vegetables and moderate in animal foods, was found in the rich rural areas. It was the largest cluster but had the lowest prevalence of glucose tolerance abnormality and was therefore used as the reference. Compared with the Green Water pattern, the New affluence pattern was associated with a substantially higher risk of glucose tolerance abnormality, independent of confounders as well as of indicators of body fatness.

The individuals with the Green Water Pattern are rice eaters foremost and have the highest consumption of vegetables and moderate use of animal food. This pattern represents the traditional Chinese diet. Our finding that the prevalence of glucose tolerance abnormalities is low in this cluster is in line with results of previous studies in different populations, which have shown an inverse association between consumption of vegetables and the risk of type 2 diabetes (8, 10, 19, 20). Unlike others (9, 10, 19), we found that fruit was located in a different dietary factor from vegetables and was positively associated with diabetes. This finding may be explained by the fact that the fruit is considered a healthy, but expensive, food in some Chinese populations.

Members of New Affluence and Western Adopter cluster are to a large extent less poor, more highly educated, and, in general, living in urban areas. They can afford more expensive foods. These Chinese individuals have benefited most from the dramatically enhanced economic opportunities, and they have broken away with the traditional Chinese food culture. As the classic food pattern shifts, intakes of cereals, vegetables and many lower-fat, mixed dished are being replaced, animal food are becoming popular, and the consumption of edible oil is increasing quickly. High consumption of animal foods is probably accompanies by a greater intake of saturated fatty acids, which may increase the risk of diabetes (21-23). Western studies showed that the Western dietary pattern, characterized by higher intakes of red and processed meat, sweets and desert, may increase the risk of type 2 diabetes (11, 21).

The Yellow Earth pattern is a typical Chinese high- carbohydrate diet, which consists of a variety of cereal products and tubers, contributing as the primary source of caloric intake. The Yellow Earth pattern is characterized by the highest intake of staples compared with the other three patterns. A high intake of staples was associated with the risk of developing type 2 diabetes in China (24). The members of the Yellow Earth cluster were primarily concentrated in the Northwest rural areas in China. Malnutrition and over-nutrition coexist in this area. This is a vulnerable group that deserves special attention from researchers and policymakers.

In our study, the association between dietary patterns and glucose tolerance abnormalities was attenuated after adjustment for lifestyle and social-economic factors. Because obesity may be an intermediate step in the pathway between diet and type 2 diabetes, one can argue that the models adjusted for BMI or WHtR present an over-adjustment. After adjustment for obesity, the elevated risk disappeared in the Yellow Earth and Western adopter cluster but remained significant in the New Affluence cluster. Thus, body fatness may partly mediate the association between diet and glucose tolerance abnormalities and from a public health point of view, the elevated risks in the Yellow Earth and New Affluence cluster are certainly relevant, as they identify high-risk groups. However, after taking into account overall overweight or abdominal obesity, the risk remains elevated in the New Affluence cluster. This finding supports the independent effect of diet on glucose metabolism and warrants even more public health attention to this dietary pattern. Adjustment for body fatness is often also used for methodological reasons. Because BMI and waist are important predictors of glucose tolerance and diabetes, the statistical efficiency of a model is improved by adding these important determinants. In addition, overweight subjects are in general known to selectively report their dietary intake, which is also possibly true in China, and including BMI in a model may partly account for this. However, residual confounding may have been present, resulting in under-adjustment as BMI or WHtR because body fatness and composition were estimated rather than perfectly measured using these anthropometric indicators.

The strengths of this study include the extensive information on diet and lifestyle, the high quality of the data collected, and the national representative sample size available for analysis that has allowed us to assess the risk of development glucose tolerance abnormalities in the general Chinese population. Another strength is the statistical technique that combined factor analysis and cluster analysis to identify Chinese dietary patterns. Factor analysis is widely used to reduce data and to extract a small number of factors depending on the correlation matrix, whereas cluster analysis is performed to further classify elements of different sources on the basis of their similarities. Cluster analysis based on factor analysis can better embody the effect of every diet factor.

There are also some limitations. First, by using a cross-sectional study, we cannot formally draw conclusions about causality. However, it should be noted that when diet and non-clinically diagnosed glucose abnormalities are investigating, it is unlikely that reverse causality has played a role. Second, dietary intake was assessed by a single food frequency questionnaire referring to a period of 1 year. Dietary habits may change over lifetime and these changes in dietary habits may have had an additional impact on diabetes. Above all, after rapid economic and social changes, Chinese dietary patterns and lifestyle have changed substantially, and an unbalanced dietary pattern, including under-nutrition and over-nutrition, may increase the risk of development of type 2 diabetes in China. Another limitation of present study is the low response rate for OGTT. The individuals whose fasting glucose level <6.1 mmol/l and 2-h glucose level >7.8 mmol/l were misclassified from glucose tolerance abnormalities to normal. This may have diluted the association between dietary pattern and glucose tolerance abnormalities. However, the amount of misclassification is likely to have been relatively small. Among the 31% of subjects who underwent an OGTT, only 8% were found to have IGT or diabetes. In addition, subgroup analysis with or without subjects who were tested for glucose tolerance did not change our results.

As the number of diabetic patients has already been estimated to be >20 million in 2002, we can expect a considerable public health burden in the near future in China and prevention is urgently warranted. Analysis of the dietary patterns and food factors that are related to the presence of glucose tolerance abnormalities, i.e., newly diagnosed diabetes and pre-diabetes, will provide the basis for future prevention studies and thereafter hopefully prevention action.

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**Appendix 1: Factor Analysis Structure Matrix**

| | Component | | | |
|---|---|---|---|---|
| | 1 | 2 | 3 | 4 |
| **Yogurt** | .666 | .109 | -.014 | .018 |
| **Milk** | .597 | .106 | .251 | -.026 |
| **Beverge** | .547 | -.093 | .085 | .096 |
| **Cheese** | .544 | .122 | -.236 | -.018 |
| **Juice** | .540 | -.020 | .197 | .077 |
| **Beef/Lamb** | .497 | .093 | .439 | .237 |
| **Cake** | .476 | .039 | .332 | .122 |
| **Milk Power** | .435 | .114 | .091 | -.009 |
| **Nut** | .385 | .020 | .248 | .226 |
| **Organ meat** | .334 | -.215 | .249 | .319 |
| **Dry bean** | .318 | -.011 | .227 | .196 |
| **Wheat** | .026 | .809 | .005 | -.007 |
| **Rice** | -.095 | -.788 | .080 | .126 |
| **Other cereal** | .092 | .646 | .050 | .004 |
| **Tubers** | -.003 | .530 | .051 | .107 |
| **Fried wheat** | .248 | .471 | .208 | .153 |
| **Vegetable** | -.121 | -.322 | .275 | .111 |
| **Seafood** | .236 | -.408 | .605 | .161 |
| **Fruit** | .257 | .172 | .595 | -.005 |
| **Poulty** | .364 | -.314 | .586 | .214 |
| **Soybean products** | .184 | .025 | .578 | .068 |
| **Egg** | .096 | .311 | .558 | .039 |
| **Pork** | .145 | -.369 | .519 | .170 |
| **Dry vegtable** | -.041 | .120 | .272 | .252 |
| **Beer** | .121 | -.016 | .130 | .766 |
| **High degree alcohol** | -.057 | .008 | .047 | .634 |
| **Low degree alcohol** | .033 | .003 | -.008 | .626 |
| **Wine** | .294 | .033 | .073 | .379 |

Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.

**Appendix 2: Final Cluster Centres in K-means Cluster procedure**

| | Cluster | | | |
|---|---|---|---|---|
| | **1** | **2** | **3** | **4** |
| **Rice** | 3.37 | 1.56 | 1.97 | 2.46 |
| **Wheat** | 1.56 | 3.29 | 2.90 | 2.39 |
| **Other cereal** | 1.51 | 3.05 | 2.72 | 2.57 |
| **Tubers** | 1.93 | 2.88 | 2.67 | 2.47 |
| **Fried wheat** | 1.59 | 2.41 | 2.76 | 2.81 |
| **Pork** | 2.73 | 1.70 | 2.69 | 3.03 |
| **Beef/Lamb** | 1.97 | 1.69 | 3.24 | 3.18 |
| **Poultry** | 2.53 | 1.48 | 2.90 | 3.16 |
| **Organ meat** | 2.37 | 1.42 | 2.43 | 3.02 |
| **Seafood** | 2.68 | 1.49 | 2.80 | 3.10 |
| **Milk** | 1.09 | 1.13 | 2.41 | 2.37 |
| **Milk power** | 1.08 | 1.15 | 1.46 | 1.71 |
| **Cheese** | 1.01 | 1.04 | 1.20 | 1.21 |
| **Yogurt** | 1.05 | 1.10 | 1.55 | 1.98 |
| **Egg** | 1.94 | 2.28 | 2.98 | 2.75 |
| **Dry bean** | 1.80 | 1.56 | 2.01 | 3.00 |
| **Vegtable** | 2.87 | 2.00 | 2.42 | 2.55 |
| **Cake** | 1.90 | 1.75 | 2.65 | 3.41 |
| **Fruit** | 1.98 | 2.07 | 2.98 | 3.05 |
| **Nuts** | 1.80 | 1.57 | 2.36 | 3.07 |
| **Low degree alcohol** | 1.31 | 1.21 | 1.27 | 1.53 |
| **High degree alcohol** | 1.37 | 1.25 | 1.32 | 1.46 |
| **Beer** | 1.42 | 1.21 | 1.38 | 2.10 |
| **Wine** | 1.03 | 1.02 | 1.07 | 1.46 |
| **Juice** | 1.29 | 1.24 | 1.36 | 3.37 |
| **Beverage** | 1.42 | 1.18 | 1.36 | 3.13 |
| **Dry vegtable** | 2.40 | 2.38 | 2.63 | 2.69 |
| **Soybean products** | 2.22 | 1.97 | 2.80 | 2.97 |

# CHAPTER 4

## Association between High Fat/Protein-Low Carbohydrate Diet Score and Newly Diagnosed Type 2 Diabetes in Chinese Population

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## Abstract

**Objective:** To study the association between High fat/protein-Low CHO score and newly diagnosed type 2 diabetes in Chinese population.

**Methods:** Data about 20 717 subjects aged 45-59 years from the cross-sectional 2002 China National Nutrition and Health Survey were analyzed. High fat/protein-Low CHO diet was scored according to the energy of carbohydrate, fat and protein.

**Results:** Of the 20 717 subjects, 1 332 were diagnosed with hyperglycemia and 662 were newly diagnosed with type 2 diabetes. Multivariate adjusted analysis showed that the highest score of type 2 diabetes patients was 2.75 (95% CI: 2.09-3.61). The score of type 2 diabetes patients was 1.87 (95%CI: 1.35-2.58) after further adjustment for their socioeconomic status and physical activity. No significant difference was found in the odds ratio after further adjustment for BMI, blood pressure, lipid level and energy intake. No evidence was observed for a relation between High fat/protein-Low CHO score with type 2 diabetes patients due to high family income, less education, physical activity, overweight, hypertension, high TG or low HDL level.

**Conclusions:** High fat/protein-Low CHO diets, far different from traditional Chinese diets, are associated with the high incidence of type 2 diabetes in Chinese population.

## Introduction

Theoretically, the traditional Chinese diet, characterized by a high intake of plant foods, high carbohydrate intake and very low dietary fat, has a potential to protect the heart. However, this potential protective effect is reducing because of a rapid change to a Western style diet with the economic transition. Dietary fat provides only 11%-22% energy for the Chinese population in the 1980s when also no significant correlation was found between dietary fat intake and body weight (1, 2). The average energy intake from fat increased from 21.8% in 1991 to 22.2% in 1993, and from 25.8% in 1997 to 28.9% and 29.6% in 2000 and 2002. Meanwhile, the proportion of total dietary energy intake from carbohydrate decreased from 65.6% in 1991 to 65.0% in 1993, and from 61.9% in 1997 to 58.8% and 58.6% in 2000 and 2002 (3, 4). During these years, the prevalence of type 2 diabetes and its related factors including obesity, hypertension and dyslipidemia has dramatically increased. The most recent data indicate that the prevalence of diabetes in Chinese adults has reached 9.7% with another 15.5% being diagnosed with either impaired fasting glucose or glucose tolerance (5).

Whether the nutrition transition from high carbohydrate-low fat diet to the opposite increases the trend of diabetes and its related factors is still unknown, because these dietary changes were accompanied by increasing sedentary lifestyle and a reduction in infectious diseases, which may also lead to chronic disease risks. A modest but significant independent effect of energy from fat on BMI has been found in Chinese adults (6). However, information about the role of a High fat/protein-Low CHO diet in diabetes is so far limited in China.

The present study aims to investigate the association between High fat/protein-Low CHO diet score and newly diagnosed type 2 diabetes in China using the cross-sectional data from 2002 China National Nutrition and Health Survey (CNNHS).

## Subjects and Methods

*Study Population*

The 2002 CNNHS was a national representative cross-sectional study on nutrition and chronic diseases. A stratified multistage probability cluster sampling design was used in this survey (4, 7). The county was divided into 6 strata according to its socioeconomic characteristics. In the first stage of sampling, 22 counties were randomly selected from each of the 6 strata. In the second stage, 3 townships were randomly selected from each of the selected counties. Two residential villages were randomly selected from each township and 90 households were randomly sampled from each village for physical examination. A total of 795 residential committees or villages and 68,828 families were sampled. About one-third of the 90 households were randomly selected to participate in the dietary survey and blood was drawn for the measurement of fasting blood glucose and lipid levels. The response rate was 87% (7). Oral glucose tolerance (OGT) was tested in subjects with their fasting glucose level ≥5.5 mmol/L.

The diet and blood glucose data about 21 390 subjects aged 45-59 years and 673 subjects with diabetes were excluded in this study. The final number of subjects in this study was 20 717. The survey protocol was approved by the Ethical Committee of the National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. All subjects signed their consent form.

*Dietary Assessment*

Trained interviewers interviewed with the subjects at their home about their food intake in the last 24 h, once a day for 3 consecutive days using the dietary recall method. The interviewers weighed the cooking oil and condiment consumed by all family members during the 3 days. The percentage of oil and condiments the subjects consumed was calculated as the ratio of his/her energy intake divided by the energy intake of all family members. The energy and nutrient intake were calculated according to the data listed on the China Food Composition Table (8).

*Calculation of the High fat/protein-Low CHO Score*

The High fat/protein-Low CHO diet score, also known as “low-carbohydrate diet score” was calculated with the method developed by Halton et al (9). Since the diet of Chinese subjects with the highest score did not include a very low carbohydrate intake as compared to the general low carbohydrate diet (10), but included a relatively high fat intake, the score was termed as “High fat/protein-Low CHO score”.

The subjects included in this study were divided into 11 strata as described by Halton et al. (9). Fat and protein intake was scored as 10, 9, 8, 7, 6, 5, 4, 3, 2, 1, and 0 respectively while the carbohydrate intake was scored as 0, 1, 2, 3, 4, 5,6, 7, 8, 9 and 10 respectively in men and women **(Table 4.1)**. The scores of fat, protein and carbohydrate intake were summed to express the overall High fat/protein-Low CHO score (range 0-3). The animal and plant High fat/protein-Low CHO scores were recorded as described by Halton et al.(9).

**Table 4.1** Criteria for Determining High fat/protein-Low CHO Diet Score

| Points | CHO intake | Total protein intake | Total fat intake | Animal-protein intake | Animal-fat intake | Vegetable-protein intake | Vegetable-fat intake |
|---|---|---|---|---|---|---|---|
| Men | | | | **percentage of energy** | | | |
| 0 | >73.5 | <8.7 | <15.1 | 0 | <0.4 | <5.8 | <3.9 |
| 1 | 69.5-73.5 | 8.7-9.5 | 15.1-18.8 | 0.1-0.5 | 0.4-2.2 | 5.8-6.5 | 3.9-8.0 |
| 2 | 66.3-69.4 | 9.6-10.1 | 18.9-22.0 | 0.6-1.1 | 2.3-4.4 | 6.6-7.1 | 8.1-11.1 |
| 3 | 63.3-66.2 | 10.2-10.6 | 22.1-25.0 | 1.2-1.7 | 4.5-6.6 | 7.2-7.6 | 11.2-13.7 |
| 4 | 60.2-63.2 | 10.7-11.2 | 25.1-27.7 | 1.8-2.3 | 6.7-8.7 | 7.7-8.1 | 13.8-16.0 |
| 5 | 57.2-60.1 | 11.3-11.7 | 27.8-30.4 | 2.4-3.0 | 8.8-10.9 | 8.2-8.6 | 16.1-18.4 |
| 6 | 54.2-57.1 | 11.8-12.4 | 30.5-33.3 | 3.1-3.7 | 11.0-13.4 | 8.7-9.1 | 18.5-21.0 |
| 7 | 50.8-54.1 | 12.5-13.0 | 33.4-36.7 | 3.8-4.6 | 13.5-16.2 | 9.2-9.7 | 21.1-23.9 |
| 8 | 46.7-50.7 | 13.1-14.1 | 36.8-40.7 | 4.7-5.8 | 16.3-20.0 | 9.8-10.5 | 24.0-27.6 |
| 9 | 40.9-46.6 | 14.2-15.9 | 40.8-46.4 | 5.9-7.5 | 20.1-25.6 | 10.6-11.4 | 27.7-33.4 |
| 10 | <40.9 | >15.9 | >46.4 | >7.5 | >25.6 | >11.4 | >33.4 |
| Women | | | | **Percentage of energy** | | | |
| 0 | >73.3 | <8.8 | <15.1 | 0 | 0 | <6.0 | <4.3 |
| 1 | 69.2-73.3 | 8.8-9.6 | 15.1-19.0 | 0.1-0.4 | 0.1-2.1 | 6.0-6.7 | 4.3-8.5 |
| 2 | 65.8-69.1 | 9.7-10.3 | 19.1-22.4 | 0.5-1.0 | 2.2-4.2 | 6.8-7.3 | 8.6-11.7 |
| 3 | 62.6-65.7 | 10.4-10.8 | 22.5-25.3 | 1.1-1.7 | 4.3-6.3 | 7.4-7.8 | 11.8-14.3 |
| 4 | 59.6-62.5 | 10.9-11.4 | 25.4-28.1 | 1.8-2.3 | 6.4-8.4 | 7.9-8.2 | 14.4-16.6 |
| 5 | 56.4-59.5 | 11.5-11.9 | 28.2-30.9 | 2.4-3.0 | 8.5-10.6 | 8.3-8.7 | 16.7-19.0 |
| 6 | 53.3-56.3 | 12.0-12.5 | 31.0-34.1 | 3.1-3.8 | 10.7-13.2 | 8.8-9.3 | 19.1-21.6 |
| 7 | 49.9-53.2 | 12.6-13.3 | 34.2-37.4 | 3.9-4.7 | 13.3-15.9 | 9.4-9.9 | 21.7-24.6 |
| 8 | 45.7-49.8 | 13.4-14.3 | 37.5-41.4 | 4.8-5.8 | 16.0-19.8 | 10.0-10.6 | 24.7-28.4 |
| 9 | 39.9-45.6 | 14.4-16.1 | 41.5-47.1 | 5.9-7.6 | 19.9-25.5 | 10.7-11.6 | 28.5-34.6 |
| 10 | <39.9 | >16.1 | 47.1 | >7.6 | >25.5 | >11.6 | >34.6 |

*Outcome Assessment*

Blood was drawn from the subjects 10–14 h after fasting plasma glucose level in fasting blood sample was measured with a spectrophotometer within 4 h after blood collection. Oral glucose tolerance was tested in subjects when fasting plasma glucose levels were ≥5.5 mmol/L. The WHO Expert Committee-recommended criteria for diabetes mellitus were used in diagnosis of diabetes (11). Hyperglycaemia was defined as fasting plasma glucose (FPG) level ≥6.1mmol/L and/or 2-h plasma glucose level ≥7.8 mmol/L. Type 2 diabetes was defined as FPG ≥7 mmol/L and/or 2-h plasma glucose ≥11.1 mmol/L. Subjects with diagnosed type 2 diabetes before this survey were excluded from this study (11).

*Measurement of Non-dietary Factors*

Information about current smoking and drinking was collected by face to face interview with the subjects. Current smoking was identified as having smoked at least one piece a week in the past 30 days, and alcohol drinking was identified as having drunk alcohol at least once a week. Sedentary activity was investigated with a questionnaire designed to collect the information of usual physical activity during one year preceding the examination. Physical activity was recorded as a 3-level variable (light, moderate and heavy) recommended by the China Nutrition Society (12), to reflect the total energy expenditure.

Fasting body weight was measured in the morning to the nearest 0.10 kg with a balance-beam scale while the subjects wore only light weight clothing. Body height of bare footed subjects was measured to the nearest 0.1 cm with a standard steel strip stadiometer. BMI ($kg/m^2$) was calculated according from body weight and height. Obesity was defined as BMI ≥28kg/m2 (13).

Plasma total cholesterol (TC), triglyceride (TG) and HDL-C levels were measured with a Hitachi 7060 or 7180 auto-analyzer (Hitachi, Tokyo, Japan). LDL level was calculated by using Friedewald formula. High TG level was defined as ≥1.7 mmol/L, low HDL-c level as <1.03 mmol/L in men and <1.29 mmol/L in women (14) and high LDL level as ≥3.62 mmol/L [15].

Resting blood pressure of the subjects was measured twice with its mean value was recorded. Hypertension was defined as systolic blood pressure (BP) ≥130 mmHg and/or diastolic BP ≥85 mmHg (14).

*Statistical Method*

The subjects were divided into quintiles of the High fat/protein-Low CHO diet score. The odds of hyperglycemia and type 2 diabetes calculated in a specific quintile was compared with that for the lowest quintile. Sex, family history of diabetes, educational level, current smoking, alcohol use, sedentary activity time and physical activity level, BMI, SBP, TG, LDL and HDL were included in the multivariate models. The subjects were stratified according to their sex, overweight, family income, educational level, sedentary activity time and physical activity level. Interaction between the High fat/protein-Low CHO diet score and stratified variables was tested by adding a multiplicative factor in the logistic regression model.

## Results

The average High fat/protein-Low CHO score ranged from 5 in lowest quintile to 25 in the highest quintile. The mean energy of fat and carbohydrate was 16.7% and 72.5% respectively in the lowest quintile, and was 42.2% and 42.9% respectively in the highest quintile **(Table 4.2)**.

*Food and Nutrient Intake in different High fat/protein-Low CHO Score*

The subjects with a higher High fat/protein-Low CHO score tended to consume less grain food and more red meat with a lower cereal fiber and dietary glycemic load, and a higher dietary fat including unsaturated fat **(Table 4.2).**

*Characteristics in different High fat/protein-Low CHO Score*

The subjects with a higher High fat/protein-Low CHO diet score drank more alcohol and smoked less and had a higher family income and educational level with a lower day time physical activity level, a longer leisure time and a sedentary activity time **(Table 4.3)**. The High fat/protein-Low CHO score was positively associated with the BMI, plasma TG and LDL level and negatively associated with the blood pressure and HDL level after adjustment for age, sex and socioeconomic status **(Table 4.3)**. Further analysis showed that the LDL increased 1.19-fold with increasing quintile of the High fat/protein-Low CHO diet score (95% CI: 1.68-2.95, $P$<0.001). The TG and HDL levels were significantly lower the odds ratio for high TG was 0.96 (95%CI: 0.93-0.99, $P$=0.011) and 0.88 ( 95%CI: 0.86-0.91, $P$<0.001) for low HDL comparing the highest to the lowest high-fat/protein-low-CHO score. However, the score was not significantly associated with obesity or hypertension in the subjects after adjustment for their socioeconomic variables.

*Association between Newly Diagnosed Hyperglycaemia and Type 2 Diabetes with High fat/protein-Low CHO Score*

Of the 20 717 subjects, 1 332 were diagnosed with hyperglycaemia and 662 with type 2 diabetes. Sex- and age-adjusted analysis showed that the odds of type 2 diabetes in the subjects with a highest quintile of the High fat/protein-Low CHO diet score was 2.75 (95% CI: 2.09-3.61) times higher than in the lowest quintile and decreased to 1.87 (95CI: 1.35-2.58) after further adjustment for socioeconomic status and physical activity. After further adjustment for BMI, blood pressure, total caloric intake and lipid levels, the odds ratio was 1.88 ( 95%CI: 1.34-2.64,**Table 4.4**).

Type 2 diabetes was also significantly associated with the High fat/protein-Low CHO score based on animal fat and protein in the sex- and age-adjusted analysis, the odds ratio was 1.74 (95%CI:1.36-2.24) in the subject with a highest quintile of the score. After further adjustment for their socioeconomic status and physical activity level, the odds ratio was 1.07 (95%CI: 0.80-1.43) **(Table 4.4)**.

The stratified analysis showed no evidence for effect modification of the relation between High fat/protein-Low CHO score and prevalence of diabetes and hyperglycemia by high family income, less education, physical inactivity, overweight, hypertension, high TG level or low HDL level in the subjects **(Table**

**4.5)**. The prevalence of type 2 diabetes increased with increasing High fat/protein-Low CHO score especially in subjects who were sedentary , overweight with a low HDL level. However, the interaction terms were not statistically significant

## Discussion

This cross-sectional survey showed that the High fat/protein-Low CHO score was associated with type 2 diabetes mellitus and hyperglycemia in the Chinese population, which was partly reduced after adjustment for their socioeconomic status and physical activity.

Theoretically, a high fat diet can increase the risk of type 2 diabetes because it reduces the expression of glucose sensing gene, glucose transporter 2 (GLUT2), glucokinase (GK), and impairs insulin secretion (15). Furthermore, oxidative stress becomes severer in subjects after having a high fat diet, which may impair beta-cell function (16), while high carbohydrate diet may speed up an age-related decline in insulin secretion and lead to an earlier onset of type 2 diabetes because high carbohydrate intake increases the requirement for insulin secretion in order to maintain glucose homeostasis and repeatedly stimulates high insulin output (16). So the optimal ratio of carbohydrate to fat in diet for diabetes prevention is not known.

There is evidence that a high carbohydrate intake decreases the prevalence of diabetes (17, 18). It was reported that replacing fat with carbohydrate significantly elevates not only postprandial glucose level but also postprandial and fasting insulin levels in patients with type 2 diabetes when the total energy intake is consistent (19). However, Bessesen (20) did not find any association between total carbohydrate and diabetes risks after reviewing the updated literature. On the contrary, a prospective study showed that low carbohydrate diets with vegetable sources of fat and protein can modestly reduce the risk of diabetes (21).

Carbohydrate in Chinese diets is commonly characterized and dominated by refined carbohydrate with a high glycemic index. Coincidentally, the majority of fat in Chinese diets are MUFA and PUFA. Such a High fat/protein-Low CHO diet should potentially protect subjects against type 2 diabetes. However, the High fat/protein-Low CHO score was significantly associated with high prevalence of type 2 diabetes in the present study. It was reported that a higher percentage of energy intake from cereals is associated with a lower risk of diabetes while a higher percentage of energy intake from fat is related with a higher likelihood of diabetes in Chinese populations (22).

**Table 4.2** Food and Nutrient Intake according to High fat/protein-Low CHO Score

| | Intake of Carbohydrate, Total Protein and Total Fat | | | Intake of Carbohydrate, Animal Protein and Animal Fat | | | Intake of Carbohydrate, Plant Protein and Plant Fat | | |
|---|---|---|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| High fat/protein-Low CHO Score | | | | | | | | | |
| Median | 5 | 15 | 25 | 3 | 16 | 25 | 8 | 15 | 21 |
| Interquartile range | 4-6 | 14-16 | 23-27 | 1-5 | 14-17 | 24-27 | 7-9 | 14-16 | 20-23 |
| No. of participants | 3911 | 4306 | 4431 | 3890 | 4846 | 4273 | 4430 | 3984 | 4547 |
| Rice and rice product (g/day) | 265±217 | 227±171 | 196±122 | 165±194 | 247±176 | 223±128 | 362±168 | 194±162 | 163±132 |
| Wheat flour and its product (g/day) | 182±202 | 155±164 | 104±100 | 277±217 | 129±140 | 85±88 | 62±104 | 181±180 | 165±150 |
| Fruit and vegetable (g/day) | 328±190 | 326±191 | 339±180 | 312±186 | 330±190 | 339±181 | 350±192 | 325±191 | 321±182 |
| Red meat (g/day) | 14.4±28.9 | 63.0±60.2 | 109±81.0 | 3.1±9.9 | 58.0±46.2 | 134±82.2 | 69.8±78.5 | 63.4±69.9 | 59.2±60.6 |
| Vegetable cooking oil (g/day) | 31.3±24.8 | 48.4±35.8 | 49.8±31.9 | 31.4±29.5 | 39.3±42.5 | 38.6±32.0 | 14.0±24.3 | 35.1±24.0 | 63.9±47.5 |
| Calories (kcal/day) | 2237±621 | 2292±689 | 2104±690 | 2187±612 | 2282±694 | 2204±726 | 2355±664 | 2231±660 | 2192±745 |
| Cereal fiber (g/day) | 7.5±5.8 | 5.5±4.9 | 3.3±3.7 | 9.0±6.2 | 5.0±4.5 | 3.3±4.0 | 4.8±4.9 | 6.3±5.7 | 4.7±4.7 |
| Glycemic index | 67.5±11.7 | 65.3±11.6 | 59.0±12.1 | 63.2±12.2 | 65.5±12.1 | 61.4±12.5 | 72.2±9.1 | 63.0±12.0 | 58.3±12.2 |
| Glycemic load | 269±87 | 212±75 | 134±64 | 244±85 | 212±84 | 148±73 | 268±85 | 204±77 | 146±69 |
| Saturated fat (% of Energy) | 8.7±5.4 | 11.9±8.8 | 11.1±6.5 | 8.1±3.9 | 12.1±8.5 | 12.0±10.1 | 12.0±11.2 | 9.8±6.5 | 13.4±7.9 |
| Monounsaturated fat (% of Energy) | 14.6±8.3 | 23.0±15.5 | 23.8±14.2 | 16.2±10.7 | 23.7±17.9 | 23.6±16.6 | 16.7±12.4 | 19.7±12.1 | 31.5±22.1 |
| Polyunsaturated fat (% of Energy) | 11.9±7.5 | 18.4±12.3 | 23.3±13.4 | 15.6±9.5 | 19.6±15.4 | 19.5±12.8 | 8.9±5.3 | 17.6±8.3 | 30.6±18.0 |
| Carbohydrate (% of Energy) | 72.9±4.3 | 57.9±4.3 | 42.9±6.8 | 71.4±5.9 | 57.5±7.8 | 43.4±7.6 | 66.0±9.5 | 59.0±9.2 | 45.9±9.4 |
| Total protein (% of Energy) | 10.3±1.4 | 11.6±2.5 | 14.7±3.0 | 10.8±1.7 | 11.7±2.7 | 14.0±3.6 | 10.6±2.2 | 12.2±2.6 | 13.0±3.7 |
| Animal protein (% of Energy) | 0.8±1.0 | 3.0±2.1 | 6.7±3.0 | 0.3±0.5 | 3.1±1.7 | 7.0±2.9 | 2.8±2.5 | 3.3±3.1 | 3.9±3.0 |
| Plant protein (% of Energy) | 9.5±1.6 | 8.6±2.0 | 8.0±2.4 | 10.5±1.7 | 8.6±2.0 | 7.0±2.0 | 7.8±1.5 | 8.8±2.1 | 9.0±2.6 |
| Total fat (% of Energy) | 16.7±4.9 | 30.3±6.4 | 42.2±7.6 | 17.6±6.2 | 30.6±8.9 | 42.4±8.3 | 23.2±9.6 | 28.6±9.1 | 41.0±10.0 |
| Animal fat (% of Energy) | 5.4±6.1 | 12.0±9.2 | 16.8±9.0 | 1.8±2.6 | 11.3±6.8 | 22.1±9.0 | 16.1±11.5 | 10.8±9.4 | 9.0±6.8 |
| Plant fat (% of Energy) | 11.3±6.2 | 18.2±9.8 | 25.4±10.3 | 15.8±7.3 | 19.3±12.3 | 20.3±10.9 | 7.0±4.8 | 17.7±5.0 | 32.0±9.7 |

***Note.*** Tested trends were all significant ($P<0.05$) except for the daily caloric intake for the animal High fat/protein-Low CHO Score.

**Table 4.3** Characteristics of Participants according to High fat/protein-Low CHO Score

| | **Intake of Carbohydrate, Total Protein and Total Fat** | | | **Intake of Carbohydrate, Animal Protein and Animal Fat** | | | **Intake of Carbohydrate, Plant Protein and Plant Fat** | | |
|---|---|---|---|---|---|---|---|---|---|
| | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 | Quintile 1 | Quintile 3 | Quintile 5 |
| Women (%) | 52.8 | 52.7 | 51.7 | 51.9 | 52.1 | 51.9 | 52.0 | 52.6 | 51.7 |
| Age (yr) | 54.4±6.7 | 54.4±6.9 | 55.4±7.2 | 54.4±6.7 | 54.8±7.0 | 54.9±7.0 | 54.3±6.8 | 54.6±6.9 | 55.4±7.1 |
| Sedentary activity time (hours/day) | 1.8±1.3 | 2.3±1.5 | 3.1±1.8 | 1.9±1.3 | 2.4±1.6 | 3.0±1.8 | 1.9±1.4 | 2.4±1.5 | 2.8±1.8 |
| Smoking (%) | 32.6 | 31.0 | 28.8 | 32.2 | 30.8 | 29.7 | 32.8 | 31.0 | 29.1 |
| Alcohol drinking (%) | 23.2 | 24.3 | 24.7 | 18.4 | 25.2 | 26.7 | 29.4 | 23.0 | 22.5 |
| Family income (Yuan/Year/Person) | | | | | | | | | |
| <800 | 25.0 | 13.5 | 4.3 | 25.7 | 11.4 | 5.8 | 19.2 | 12.2 | 8.8 |
| 800-1999 | 45.3 | 29.1 | 11.5 | 44.8 | 27.5 | 15.3 | 40.0 | 31.6 | 17.5 |
| 2000-4999 | 24.6 | 32.9 | 24.9 | 24.2 | 32.7 | 26.3 | 29.4 | 28.9 | 27.7 |
| ≥5000 | 5.1 | 24.5 | 59.3 | 5.3 | 28.4 | 52.7 | 11.5 | 27.4 | 46.1 |
| Education | | | | | | | | | |
| Illiterate | 25.6 | 17.7 | 6.9 | 25.5 | 16.6 | 8.2 | 23.8 | 16.0 | 11.2 |
| Primary school | 47.0 | 39.3 | 26.3 | 43.9 | 38.9 | 29.9 | 46.5 | 38.3 | 29.8 |
| Middle school (Junior or senior) | 26.8 | 39.9 | 56.3 | 30.1 | 40.5 | 52.9 | 28.6 | 41.1 | 51.3 |
| College or above | 0.6 | 3.2 | 10.6 | 0.6 | 4.1 | 9.0 | 1.1 | 4.6 | 7.8 |
| Low activity level (%) | | | | | | | | | |
| Low | 22.1 | 43.2 | 78.1 | 23.7 | 47.5 | 72.1 | 27.3 | 48.1 | 65.7 |
| Medium | 28.4 | 24.7 | 14.1 | 29.9 | 22.5 | 15.2 | 25.8 | 23.6 | 18.3 |
| High | 49.5 | 32.2 | 7.8 | 46.4 | 30.0 | 12.7 | 47.0 | 28.3 | 16.1 |
| Body mass index ($kg/m^2$) [1] | 23.3±3.7 | 23.7±3.5 | 23.8±3.9 | 23.8±3.7 | 23.6±3.5 | 23.3±3.7 | 22.7±3.6 | 23.7±3.5 | 24.1±3.6 |
| Low density lipoprotein (mmol/L) [1] | 2.09±0.83 | 2.19±0.79 | 2.36±0.86 | 2.07±0.83 | 2.22±0.0.79 | 2.35±0.83 | 2.22±0.82 | 2.20±0.79 | 2.28±0.81 |
| High density lipoprotein (mmol/L) [1] | 1.27±0.34 | 1.32±0.32 | 1.34±0.35 | 1.25±0.34 | 1.33±0.0.32 | 1.37±0.34 | 1.34±0.34 | 1.30±0.32 | 1.31±0.33 |
| Triglyceride (mmol/L) [1] | 1.27±0.85 | 1.24±0.80 | 1.20±0.88 | 1.29±0.84 | 1.23±0.80 | 1.18±0.85 | 1.22±0.83 | 1.24±0.80 | 1.25±0.82 |
| Systolic blood pressure (mmHg) [1] | 130.3±23.0 | 130.3±21.7 | 128.0±23.7 | 131.3±22.7 | 129.3±21.7 | 127.0±22.9 | 127.5±22.4 | 130.1±21.7 | 130.2±22.3 |
| Diastolic blood pressure (mmHg) [1] | 81.5±12.9 | 81.6±12.1 | 81.1±13.3 | 82.3±12.7 | 81.2±12.1 | 80.4±12.8 | 79.9±12.6 | 81.6±12.1 | 82.0±12.4 |

***Note.*** [1]Adjusted means and SD, other variables in the model included sex, age in 5-y categories, current smoking (yes vs. no), and current drinking (yes vs. no), sedentary activity time in 1-h categories, family history of type 2 diabetes, family income level (four categories: <800, 800-1999, 2000-4999, ≥5000Yuan/Person/year), educational level (four categories: illiterate, primary school, middle school, colleague/university or above). Tested trends were all significant ($P$<0.05) except for triglyceride for the plant High fat/protein-Low CHO Score.

**Table 4.4** Odds Ratio (95%CI) of Newly Diagnosed Hyperglycaemia and Type 2 Diabetes according to High fat/protein-Low CHO Score

| High fat/protein-Low CHO Score | Quintile 1<br>1 | Quintile 2<br>3 | Quintile 3<br>5 | Quintile 4<br>8 | Quintile 5<br>10 | *P* for trends |
|---|---|---|---|---|---|---|
| **TYPE 2 DIABETES** | | | | | | |
| By total carbohydrate, total protein and total fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.73 (1.29-2.32) | 1.83 (1.36-2.45) | 2.03 (1.52-2.73) | 2.75 (2.09-3.61) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.62 (1.19-2.21) | 1.54 (1.13-2.11) | 1.63 (1.18-2.24) | 1.87 (1.36-2.58) | 0.0015 |
| Multivariate plus BMI [2] | 1.0 | 1.58 (1.16-2.16) | 1.43 (1.04-1.96) | 1.53 (1.10-2.11) | 1.73 (1.25-2.45) | 0.0080 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.54 (1.11-2.14) | 1.48 (1.05-2.96) | 1.66 (1.18-2.33) | 1.86 (1.32-2.61) | 0.0015 |
| By total carbohydrate, animal protein and animal fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.20 (0.91-1.57) | 1.34 (1.04-1.74) | 1.36 (1.04-1.79) | 1.74 (1.36-2.24) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.07 (0.81-1.42) | 1.00 (0.76-1.32) | 0.96 (0.71-1.29) | 1.07 (0.80-1.43) | 0.8844 |
| Multivariate plus BMI [2] | 1.0 | 1.08 (0.81-1.43) | 1.02 (0.77-1.35) | 0.99 (0.73-1.33) | 1.13 (0.84-1.51) | 05866 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.09 (0.81-1.47) | 1.13 (0.85-1.52) | 1.08 (0.79-1.49) | 1.23 (0.90-1.68) | 0.2476 |
| By total carbohydrate, plant protein and plant fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.35 (1.00-1.83) | 2.02 (1.52-2.67) | 2.38 (1.81-3.14) | 2.65 (2.03-3.44) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.32 (0.96-1.81) | 1.77 (1.31-2.39) | 1.97 (1.46-2.66) | 2.16 (1.61-2.88) | <.0001 |
| Multivariate plus BMI [2] | 1.0 | 1.13 (0.82-1.56) | 1.49 (1.09-2.81) | 1.59 (1.18-2.15) | 1.73 (1.29-2.31) | <.0001 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.18 (0.84-1.66) | 1.52 (1.10-2.09) | 1.69 (1.23-2.32) | 1.83 (1.34-2.54) | <.0001 |
| **HYPERGLYCAEMIA** | | | | | | |
| By total carbohydrate, total protein and total fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.43 (1.17-1.76) | 1.60 (1.31-1.96) | 1.73 (1.41-2.11) | 2.31 (1.92-2.79) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.35 (1.09-1.66) | 1.39 (1.13-1.72) | 1.46 (1.17-1.81) | 1.72 (1.38-2.14) | <.0001 |
| Multivariate plus BMI [2] | 1.0 | 1.30 (1.06-1.61) | 1.29 (1.04-1.65) | 1.37 (1.10-1.71) | 1.59 (1.27-1.98) | 0.0002 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.29 (1.04-1.61) | 1.32 (1.06-1.64) | 1.44 (1.15-1.81) | 1.63 (1.29-2.45) | <.0001 |
| By total carbohydrate, animal protein and animal fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.15 (0.94-1.45) | 1.34 (1.11-1.62) | 1.43 (1.18-1.73) | 1.69 (1.40-2.72) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.04 (0.85-1.27) | 1.08 (0.89-1.31) | 1.09 (0.88-1.34) | 1.17 (0.95-1.43) | 0.1318 |
| Multivariate plus BMI [2] | 1.0 | 1.05 (0.85-1.28) | 1.10 (0.90-1.34) | 1.12 (0.91-1.39) | 1.23 (1.00-1.52) | 0.0376 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.05 (0.85-1.32) | 1.16 (0.95-1.42) | 1.19 (0.95-1.48) | 1.29 (1.03-1.66) | 0.0134 |
| By total carbohydrate, plant protein and plant fat | | | | | | |
| Age and sex adjusted | 1.0 | 1.29 (1.06-1.59) | 1.72 (1.41-2.99) | 2.06 (1.70-2.49) | 2.21 (1.84-2.65) | <.0001 |
| Multivariate adjusted [1] | 1.0 | 1.25 (1.01-1.55) | 1.56 (1.28-1.92) | 1.78 (1.45-2.18) | 1.86 (1.53-2.27) | <.0001 |
| Multivariate plus BMI [2] | 1.0 | 1.10 (0.88-1.36) | 1.33 (1.08-1.63) | 1.45 (1.18-1.79) | 1.50 (1.23-1.84) | <.0001 |
| Multivariate plus BMI, SBP, TG,HDL, LDL[3] | 1.0 | 1.13 (0.91-1.42) | 1.34 (1.08-1.66) | 1.53 (1.23-1.97) | 1.55 (1.26-1.91) | <.0001 |

***Note.*** [1] Odds ratio was adjusted for sex, age in 5-y categories, current smoking (yes *vs.* no), and current drinking (yes *vs.* no), sedentary activity time in 1-h categories, family history of type 2 diabetes, family income level (four categories: <800, 800-1999, 2000-4999, ≥5000Yuan/Person/year), educational level (four categories: illiterate, primary school, middle school, colleague/university or above), [2] Further adjusted for BMI (continuous variable in each unit); [3]Further adjusted for BMI, SBP, TG, LDL, HDL (continuous).

**Table 4.5** Stratified Odds Ratio (95%CI)[1] of Newly Diagnosed Hyperglycaemia according to High fat/protein-Low CHO Score

| | Quintile | | | | | *P* for | *P* for |
|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | trends | Interaction |
| **Sex** | | | | | | | |
| Male | 1 | 1.31 (0.94-1.86) | 1.31 (0.95-1.81) | 1.39 (0.99-1.94) | 1.76 (1.26-2.45) | 0.0013 | 0.1254 |
| Female | 1 | 1.31 (0.99-1.74) | 1.30 (0.98-1.73) | 1.36 (1.01-1.82) | 1.44 (1.07-1.94) | 0.0382 | |
| **Family income (Yuan/Year/Person)** | | | | | | | |
| <2000 | 1 | 1.39 (1.07-1.80) | 1.11 (0.83-1.48) | 1.33 (0.97-1.83) | 1.50 (1.05-2.14) | 0.0637 | 0.4763 |
| ≥2000 | 1 | 1.23 (0.85-1.77) | 1.52 (1.08-2.15) | 1.44 (1.01-2.43) | 1.74 (1.24-2.44) | 0.0004 | |
| **Educational level** | | | | | | | |
| Illiterate or primary school | 1 | 1.20 (0.93-1.55) | 1.27 (0.98-1.65) | 1.41 (1.06-1.86) | 1.52 (1.13-2.43) | 0.0031 | 0.2792 |
| Middle school or colleague and above | 1 | 1.52 (1.03-2.24) | 1.34 (0.92-1.97) | 1.36 (0.92-1.99) | 1.70 (1.17-2.47) | 0.0189 | |
| **Physical activity level** | | | | | | | |
| Low | 1 | 1.26 (0.87-1.82) | 1.31 (0.92-1.86) | 1.40 (0.99-1.99) | 1.65 (1.17-2.33) | 0.0010 | 0.4528 |
| Medium | 1 | 1.48 (0.99-2.26) | 1.36 (0.89-2.55) | 1.67 (1.07-2.61) | 1.36 (0.83-2.22) | 0.1555 | |
| High | 1 | 1.26 (0.89-1.79) | 1.27 (0.88-1.84) | 0.99 (0.60-1.69) | 1.72 (1.02-2.91) | 0.1963 | |
| **Leisure sedentary activity (hours/day)** | | | | | | | |
| <2 | 1 | 1.34 (0.97-1.86) | 1.18 (0.84-1.68) | 1.31 (0.89-1.91) | 2.04 (1.40-2.98) | 0.0017 | 0.6684 |
| ≥2 | 1 | 1.31 (0.99-1.73) | 1.35 (1.03-1.78) | 1.37 (1.04-1.82) | 1.48 (1.12-1.95) | 0.0167 | |
| **BMI ($kg/m^2$)** | | | | | | | |
| ≥24 | 1 | 1.40 (1.04-1.87) | 1.37 (1.02-1.83) | 1.59 (1.19-2.14) | 1.61 (1.20-2.16) | 0.0027 | 0.9167 |
| <24 | 1 | 1.25 (0.92-1.69) | 1.30 (0.95-1.78) | 1.07 (0.75-1.52) | 1.73 (1.23-2.44) | 0.0155 | |
| **Hypertension** | | | | | | | |
| Yes | 1 | 1.32 (0.98-1.79) | 1.28 (0.95-1.73) | 1.40 (1.02-1.91) | 1.62 (1.18-2.25) | 0.0047 | 0.9790 |
| No | 1 | 1.27 (0.94-1.72) | 1.31 (0.97-1.77) | 1.35 (0.98-1.85) | 1.59 (1.16-2.18) | 0.0077 | |
| **High TG** | | | | | | | |
| Yes | 1 | 1.32 (0.88-1.97) | 1.52 (1.03-2.25) | 1.46 (0.97-2.21) | 1.57 (1.04-2.35) | 0.0536 | 0.7896 |
| No | 1 | 1.34 (1.03-1.73) | 1.26 (0.97-1.64) | 1.51 (1.16-1.96) | 1.75 (1.35-2.28) | <.0001 | |
| **Low HDL** | | | | | | | |
| Yes | 1 | 1.53 (1.10-2.12) | 1.61 (1.16-2.24) | 1.65 (1.16-2.34) | 1.87 (1.32-2.65) | 0.0017 | 0.3481 |
| No | 1 | 1.16 (0.87-1.54) | 1.11 (0.84-1.48) | 1.24 (0.92-1.66) | 1.42 (1.05-1.97) | 0.0176 | |

***Note.*** [1] Odds ratio was adjusted for sex, age in 5-y categories, current smoking (yes *vs.* no), and current drinking (yes *vs.* no), sedentary activity time in 1-h categories, family history of type 2 diabetes, family income level (four categories: <800, 800-1999, 2000-4999, ≥5000Yuan/Person/year), educational level (four categories: illiterate, primary school, middle school, colleague/university or above), BMI and physical activity level (low, medium and high). The stratification variable was excluded from the relative model.

The question is the relation between the dietary pattern and disease risks is due to differences in socioeconomic status. Socioeconomic status, physical activity, and BMI could be major confounders of this association. The multivariate model and stratified analysis showed that the High fat/protein-Low CHO diet score was significantly associated with the risk of type 2 diabetes mellitus, even after adjustment for these variables. However, residual confounding may still exist. As the vegetable cooking oil is the main source of fat for people with a high plant fat/protein-low CHO score, it does not depend on the socioeconomic level, at least not as much as the animal High fat/protein-Low CHO score, because cooking oil is quite cheap in China. The carbohydrate and animal fat and protein diet score mainly reflects a higher socioeconomic status and a sedentary life style. In our study, the association between the animal food-based diet score is significantly associated with t2d in age adjusted model but not in the model adjusted by SES. This assumption, which coincides with the association between type 2 diabetes mellitus and the animal food-based diet score is not significant any more after multivariate adjustment. It was reported that the low carbohydrate diet is associated with favorable changes in TG and HDL-C levels and unfavorable changes in LDL-C level (23), which indirectly supports the assumption that the association between diet score and diabetes should not only reflect the different socioeconomic status.

It was reported that subjects with a higher total fat intake (>37%E) do not benefit from MUFA (24), which is consistent with the fact that changes in estimated desaturase activities (derived from plasma FA composition) are related with changes in insulin sensitivity only in subjects with a total fat intake <35.5%E (25). The dietary energy intake from PUFA was over 10% (which is the recommended maximum PUFA intake level (26)) in the subjects with the lowest High fat/protein-Low CHO score.

The traditional dietary pattern of Chinese populations is characterized by high carbohydrate intake with very low fat intake, which is undergoing rapid transition to the high fat dietary pattern similar to Western countries. This transition will last a period when various dietary patterns coexist and provide the opportunity to study the association between dietary patterns and diabetes mellitus in a large range of exposed factors. As type 2 diabetes is only a recent epidemic in China, the present study offers a good window to study the associated dietary factors. Fifty percent of the subjects with diabetes in this study were not aware of the fact, supporting the assumption that these subjects still have no chance to change their diets due to type 2 diabetes mellitus or dietary treatment. Meanwhile, several weak points in this study should also be noticed. Firstly, oral glucose tolerance was not tested, which might result in an underestimation of diabetes cases and misclassification of some cases. Yang et al (5) recently reported that 46.6% of undiagnosed diabetes the cases meet the criteria for elevated 2-hour plasma glucose level in an oral glucose tolerance test but not the criteria for elevated fasting glucose levels. However, the misclassification of diabetes cases may weaken the real association but not overestimation of causes. In addition, the weaknesses of cross-section study design should not be neglected, which may limit any cause relationship linking.

In conclusion, High fat/protein-Low CHO diets, which are far different from the traditional Chinese diets, are associated with a higher risk of type 2 diabetes in China.

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# CHAPTER 5

## Dietary patterns as compared with physical activity in relation to metabolic syndrome among Chinese adults

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## Abstract

**Objective**: To examine the nationally-representative dietary patterns and their joint effects with physical activity on the likelihood of metabolic syndrome (MS) among 20,827 Chinese adults.

**Methods:** CNNHS was a nationally representative cross-sectional observational study. Metabolic syndrome was defined according to the Joint Interim Statement definition.

**Results**: The 'Green Water' dietary pattern, characterized by high intakes of rice and vegetables and moderate intakes in animal foods was related to the lowest prevalence of MS (15.9%). Compared to the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern, characterized by high intakes of refined cereal products, tubers, cooking salt and salted vegetable was associated with a significantly elevated odds of MS (odds ratio 1.66, 95%CI: 1.40-1.96), after adjustment of age, sex, socioeconomic status and life style factors. The 'Western/new affluence' dietary pattern characterized by higher consumption of beef/lamb, fruit, eggs, poultry and seafood also significantly associated with MS (odds ratio: 1.37, 95%CI: 1.13-1.67). Physical activity showed significant interactions with the dietary patterns in relation to MS risk (*P* for interaction = 0.008). In the joint analysis, participants with the combination of sedentary activity with the 'Yellow Earth' dietary pattern or the 'Western/new affluence' dietary pattern both had more than three times (95%CI: 2.8-6.1) higher odds of MS than those with active activity and the 'Green Water' dietary pattern.

**Conclusions**: Our findings from the large Chinese national representative data indicate that dietary patterns affect the likelihood of MS. Combining healthy dietary pattern with active lifestyle may benefit more in prevention of MS.

## Introduction

The metabolic syndrome (MS) is characterized by a clustering of cardiovascular risk factors, including obesity, hypertension, increased glucose concentration, and dyslipidemia. In China, the prevalence of MS and its major components have been rapidly rising, largely reflecting the transition of lifestyle and nutrition during the past two decades (1).

Dietary patterns have been widely used to identify typical combinations of foods, which have been associated with MS in different populations (2-7). A 'Western/new affluence' dietary pattern, characterized by high intakes of refined grains, processed meat, fried foods, and red meat, has been related to increased incidence of MS in Americans, Mexicans and Iran women; whilst adherence to the Mediterranean diet pattern was associated with a lower prevalence of MS. A traditional rice and beans pattern was associated with MS in Puerto Rican older adults (7).

Few studies have examined the associations between Chinese dietary patterns and MS. A Chinese traditional dietary pattern was recently associated with reduced weight gain and MS in Jiangsu province of China (8,9). In Shanghai Men's Health Study, a 'fruit and milk' pattern was associated with lower prevalence of both pre-hypertension and hypertension (10); and in Shanghai Women's Health Study, a dietary pattern low in staple foods and high in dairy milk was associated with lower risk of type 2 diabetes (11). We recently featured Chinese dietary patterns using data from China National Nutrition and Health Survey (CNNHS). In our previous analyses, we found the derived dietary patterns were associated with hyperglycemia (12) and obesity (13). However, it remains unknown whether these patterns are related to MS risk. In addition, sedentary lifestyle accompanied nutrition transition in China, few studies have examined the joint effects of unhealthy dietary patterns and sedentary lifestyle on MS risk.

Our objective of this study was to examine whether the national-representative dietary patterns were associated with MS and its components in a large sample of Chinese adults (N=20,827); and to particularly assess the interaction and joint effects of dietary patterns and physical activity on MS risk.

## Methods

*Study population*

The 2002 CNNHS is a nationally representative cross-sectional study on nutrition and chronic diseases. A stratified, multistage probability cluster sampling design was used in this survey. Based on socioeconomic characteristics, the country was divided into six regions. In the first stage of sampling, 22 counties were randomly selected from each of the 6 regions in China. In the second stage, three townships were randomly selected from each of the selected counties. From each of the townships, 2 residential villages were randomly selected; and 90 households were then randomly sampled from each village for physical examination.

A total of 795 residential committees or villages and 68,828 families were sampled. One-third of the households were selected to participate in the dietary survey and blood draw. Among the sampled family members, 12% refused to participate or had missing data. Among the subjects who finalized the food frequency questionnaire, 6% were excluded because of extreme values, including daily energy intake >5,000 kcal. For the present study, we used data of participants aged 45-69 years. The final sample size was 20,827.

The protocol of the 2002CNNHS was approved by the Ethical Committee of the National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. Signed consent forms were obtained from all participants.

*Data collection*

Participants went to the study sites for anthropometric measurements. In the morning, body weight, height and waist circumference were all measured in the fasting state by trained investigators, and duplicate measurements in subgroups showed high reproducibility. Barefoot height and fasting weight were measured to an accuracy of 1 mm and 0.1kg, respectively. The waist circumference was measured to the nearest 0.1 cm at the midpoint between the bottom of the rib cage and the top of the iliac crest at the end of exhalation.

Subjects' seated blood pressure was measured for two times using mercury sphygmomanometer on the right arm after 5 min of rest to the nearest 2 mmHg by uniform trained staffs from local Centers for Disease Control and Prevention according to 1999 World Health Organization/International Society of Hypertension guidelines on hypertension (14). The cuff size was selected on the basis of the upper arm circumference to ensure that the cuff did not overlap.

All subjects were invited for blood collection after approximately 10-14 h overnight fast. Fasting plasma glucose levels were measured with a spectrophotometer within 4 h. All individuals in present study had fasting glucose levels measured. Other plasma samples were shipped on a dry ice to Chinese Center for Disease control and Prevention, at which plasma triglyceride, total cholesterol and high density lipoprotein cholesterol were measured enzymatically with the Hitachi 7060, 7180 auto–analyzer (Hitachi, Tokyo, Japan).

*Definition of MS*

Metabolic syndrome was defined according to the most recent Joint Interim Statement (JIS) among organizations (15), as three or more of the following variables and cut-off points: (a) high fasting glucose: ≥5.6 mmol/L; (b) low HDL-cholesterol: men<1.0 mmol/L; women <1.3 mmol/L; (c) high fasting triglyceride: ≥1.7 mmol/L; (d) high blood pressure: systolic blood pressure ≥130 mmHg and/or diastolic blood pressure ≥85 mmHg. Individuals who had ever been diagnosed as diabetes or hypertension met the criteria for high blood pressure or high fasting glucose; (e) abdominal obesity: waist circumference men≥85 cm; women≥80 cm specifically for Chinese adults (16).

*Dietary patterns*

A validated semi-quantitative food frequency questionnaire was used to evaluate the usual dietary intakes in the previous 1 year before the study, in which both the frequency and the quantity of the 33 types of food categories were recorded, including rice, wheat, different types of meat, aqua-products, milk and dairy products, soy products, fresh and dried vegetables, fruits, cake, nuts, different alcohol drinks, juice, beverages, and so on.

The construction of dietary patterns using factor analysis combined with cluster analysis was described in detail elsewhere (12,13). Briefly, we first applied principal components analysis to identify 4 groups of interrelated food categories. Then, the factor scores were used in a cluster analysis and revealed a 4-cluster solution (Appendix 1, 2 , Chapter 3).

The first cluster, namely the ‘Yellow Earth’ dietary pattern (their food is mainly produced on the dry and hilly land, like the mountain area in the Northwest), was characterized by high intakes of wheat flour products and (sweet) potato, combined with low consumption of protein products such as pork, beef/lamb, poultry, seafood or milk and milk products, represented a typical traditional diet in north China. The second cluster, namely the ‘Green Water’ dietary pattern (like the rice area in the Southeast) (13,14), represented a typical traditional diet in south China, characterized by high intakes of rice and vegetables, and moderate intakes of seafood, pork and poultry. The third (‘Western’)and fourth (‘New Affluence’) clusters (12,13) were characterized by similar food combination, i.e. high consumption of beef/lamb, fruit, eggs, poultry, seafood, tofu, milk products, and cake, fruit juice, beverages, nuts, beer and wine. We therefore combined these two clusters together, named as the ‘Western/new affluence’ dietary pattern. Participants with the ‘Western/new affluence’ dietary pattern mainly lived in cities (13).

*Assessments of physical activity and covariates*

Information on physical activity was collected by trained investigators using a 1-year physical activity questionnaire (17).The frequency and duration of the five domains of physical activity were recorded. The intensity (metabolic equivalent， METs, unit kcal/kg·h) of each activity in the questionnaire was coded according to the compendium of physical activities (18). Physical activity level (6) was calculated according to the Institute of Medicine (IOM) recommendations as below (19):

Male：ΔPAL=(A METs-1)×1.34×(B min)/1440min （1.34=1.15/0.9/0.95）

Female：ΔPAL=(A METs-1)×1.42×(B min)/1440min （1.42=1.15/0.9/0.91）

PAL=1.0+ΔPAL

A: intensity of each activity; B: duration of each activity

PAL was then classified into four categories as sedentary: PAL 1.00–1.39; low active: PAL 1.40–1.59; active: PAL 1.60–1.89; and very active: PAL 1.90–2.50 (17).

Current economic status was assessed by the mean annual income in the past year before 2002CNNHS. Current smoking was identified as having smoked at least one piece a week in the past 30 days, and alcohol drinking was identified as drinking alcohol at least once per week. Salt consumption was recorded combined with weighted food method. Family history of hypertension (diabetes) was defined as yes if a family member (grandparents, parents and siblings) had ever been diagnosed with hypertension (diabetes). BMI was calculated by measured body weight and height. We used criteria recommended for Chinese adults and classified subjects as underweight, normal weight, overweight and obesity as BMI <18.5, 18.5-23.9, 24-27.9 and ≥ 28 $kg/m^2$, respectively (16).

*Statistic methods*

Survey analyses in SAS 9.2 for Windows (SAS Institute Inc, Cary, NC) were performed to estimate statistics for this complex multistage designed survey sample. Survey weights were derived from the 2000 Census and associated administrative data and used in all analyses.

The characteristics were compared between sex and the dietary patterns using the $\chi^2$ statistic for discrete variables. The mean values of the MS index were estimated using the Survey means estimates according to the dietary patterns, which was then compared using the Survey regression models after further adjusted age, sex, rural/urban, family income, educational level, current smoking, drinking, physical activity level, cooking salt and salted vegetable consumption, dietary energy intake, family history of hypertension, and family history of diabetes. The crude and multivariable adjusted odds ratios (95% CIs) of MS and its components, as well as the number of individual abnormalities between different dietary patterns were estimated using Survey logistic model. In order to assess whether the associations between dietary patterns and MS were mediated by obesity, we further included BMI (continue variable) in the model.

In order to assess the combination of energetic factors, we examined the joint association of dietary patterns and physical activity level with MS risk. We also performed stratified analysis by sex, age, rural/urban, current smoking, drinking and physical activity. We tested for interaction between those risk factors and dietary patterns by creating categorical interaction terms and comparing the log likelihood of this model with the model that contained the main effects only. In order to minimize this limitation, we did a sensitivity analysis excluding participants who were aware of their metabolic aberrations, including diabetes (n=3,359), hypertension (n=2,813) or dyslipidemia (n=1,058).

## Results

According to the JIS criteria, the prevalence of MS was 17.3% in men and 25.5% in women. High blood pressure (50.9%) was the most prevalent component of the MS, followed by central obesity (38.4%) and low HDL (32.1%). Women had a higher prevalence of central obesity and low HDL cholesterol than men **(Table 5.1)**.

Compared with people with the 'Green Water' dietary pattern, participants with both the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern had significantly higher BMI, waist circumference, blood pressure, triglyceride and lower HDL concentration. The participants with the 'Western/new affluence' dietary pattern also had a higher fasting glucose level as compared to participants with the 'Green Water' dietary pattern **(Table 5.2)**. The 'Yellow Earth' dietary pattern was associated with the highest systolic blood pressure and lowest HDL concentration, while the 'Western/new affluence' dietary pattern was associated with the highest glucose level. The prevalence of MS was 15.9%, 22.7%, and 28.7% among the participants with the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern, respectively **(Table 5.3)**.

Compared with people with the 'Green Water' dietary pattern, the multiple adjusted odds ratio of MS was 1.66 (95%CI: 1.40-1.96) for those with the 'Yellow Earth' dietary pattern and 1.37 (95% CI: 1.13-1.67) for those with the 'Western/new affluence' dietary pattern (Table 3). The associations between dietary patterns and MS were attenuated when body mass index was added to the models (Table 3). Comparing to the 'Green Water' dietary pattern, the 'Yellow Earth' and the 'Western/new affluence' dietary patterns also associated with a higher odds of having one or two MS individual abnormalities, which was independent of BMI.

**Table 5.1** Selected characteristics of Chinese adults according to dietary cluster (2002 China National Nutrition and Health Survey)

| | | Men | Women | *P*[a] |
|---|---|---|---|---|
| N (%) | | 9936 (47.7) | 10891 (52.3) | 20827 |
| Age (%) | 45~54 yrs | 53.5 | 57.1 | 0.01 |
| | 55~69 yrs | 46.5 | 42.9 | |
| Area (%) | Rural | 64.6 | 62.7 | 0.19 |
| Current smoker (%) | | 25.5 | 2.0 | <0.0001 |
| Alcohol drinker (%) | | 45.7 | 5.5 | <0.0001 |
| Physical activity level (%) | Light | 32.3 | 27.0 | <0.0001 |
| | Low active | 13.3 | 22.0 | |
| | Active | 15.2 | 16.1 | |
| | Very active | 39.2 | 34.9 | |
| Annual family income RMB/person/year (%) | <2000 | 42.4 | 41.9 | 0.94 |
| | 2000~4999 | 17.3 | 17.6 | |
| | ≥5000 | 40.3 | 40.5 | |
| Education level (%) | Illiterate | 7.6 | 25.8 | <0.0001 |
| | Primary school | 36.9 | 40.2 | |
| | High school | 50.0 | 32.0 | |
| | Above high school | 5.5 | 2.0 | |
| High blood pressure | (≥130/85mmHg) | 51.9 | 50.1 | 0.21 |
| Hypertriglyceridemia | (≥1.7 mmol/l) | 17.8 | 16.4 | 0.20 |
| Low HDL cholesterol | (<1.0/1.3 mmol/l) | 16.4 | 46.1 | <0.0001 |
| Hyperglycemia | (glucose≥5.6 mmol/l) | 12.2 | 12.1 | 0.92 |
| Central obesity | (≥85/80cm) | 34.0 | 42.3 | <0.0001 |
| MS | | 17.3 | 25.5 | <0.0001 |

[a] $\chi$-test

Specifically, when comparing to the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern was significantly associated with hypertension, central obesity and low HDL, which the 'Western/new affluence' dietary pattern was significantly associated with hyperglycemia, central obesity and low HDL independent of the common risk factors **(Table 5.3)**. When comparing the 'Yellow Earth' and the 'Western/new affluence' dietary patterns, the 'Yellow Earth' dietary pattern was associated with a relatively higher odds of hypertension and a marginally higher odds of low HDL, while the 'Western/new affluence' dietary pattern was associated with a relatively higher odds of hyperglycemia.

**Table 5.2** The adjusted mean levels of individual MS components according to dietary patterns (2002 China National Nutrition and Health Survey) [c].

| | Green Water (n=7407) | Yellow Earth (n=5677) | Western/new affluence (n=7681) |
|---|---|---|---|
| BMI (kg/m$^2$) | 22.6 (0.08) | 23.6 (0.09) [a] | 24.5 (0.08) [a] |
| Waist circumference (cm) | 76.5 (0.23) | 79.5 (0.26) [a] | 83.1 (0.25) [a] |
| Systolic blood pressure (mmHg) | 128.2 (0.52) | 131.1 (0.59) [a] | 130.8(0.53)[b] |
| Diastolic blood (mmHg) | 80.1 (0.28) | 81.5 (0.32) [a] | 82.4 (0.29) [a] |
| Triglyceride (mmol/L) | 1.18 (0.02) | 1.18 (0.01) | 1.36 (0.02) |
| High density lipoprotein (mmol/L) | 1.39 (0.01) | 1.28 (0.01) [a] | 1.29 (0.01) [a,b] |
| Fasting plasma glucose (mmol/L) | 4.92 (0.02) | 4.97 (0.02) | 5.31 (0.04) [a,b] |

[a] $P$<0.05 compared to participates with the 'Green Water' dietary pattern.
[b] $P$<0.05 compared to participates with the 'Yellow Earth' dietary pattern; Comparison further adjusted age (continue), sex, family income (<2000, 2000-4999, ≥5000 RMB/person/year), living area (urban/rural), current smoking (yes/no), drinking (yes/no), physical activity level (light, low active, active, very active), education level (Illiterate, primary, high school, above high school), cooking salt (continue) and salted vegetable (continue) consumption, dietary energy intakes (continue), family history of hypertension (yes/no) and family history of diabetes (yes/no).
[c] Means (standard error) from the weighted analysis.

In the stratified analyses **(Table 5.4)**, the associations between dietary patterns and MS were consistent in the young and the elder participates, but seems stronger among female, in rural, and in absence of smoking or drinking. In the sensitivity analysis by exclusion of participants who were aware of their diabetes, hypertension or dyslipidemia, as compared with the 'Green Water' dietary pattern, the multiple adjusted odds ratio of MS was 1.61 (95%CI: 1.31-1.97) for those with the 'Yellow Earth' dietary pattern and 1.30 (95%CI:1.02-1.66) for those with the 'Western/new affluence' dietary pattern, which was attenuated after further adjusted BMI.

**Table 5.3** Prevalence and odds ratios[a] (95% confidence intervals) of MS according to dietary patterns.

| | 'Green Water' | 'Yellow Earth' | 'Western/new affluence' | *P* |
|---|---|---|---|---|
| MS | | | | |
| Cases, n (%) | 1154 (15.9) | 1348 (22.7) | 2268 (28.7) | |
| Age and sex adjusted | 1.0 | 1.51(1.29-1.78) | 2.14(1.82-2.52) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.66(1.40-1.96) | 1.37(1.13-1.67) | 0.046 |
| +BMI adjusted | 1.0 | 1.12(0.93-1.35) | 1.03(0.82-1.30) | 0.43 |
| Individual MS component | | | | |
| High blood pressure | | | | |
| Cases, n (%) | 3392 (47.6) | 3008 (52.6) | 4232 (54.4) | |
| Age and sex adjusted | 1.0 | 1.21(1.06-1.39) | 1.33(1.16-1.53) | 0.16 |
| Multivariable adjusted[a] | 1.0 | 1.28(1.11-1.47) | 1.05(0.90-1.22) | 0.01 |
| +BMI adjusted | 1.0 | 1.04 (0.90-1.20) | 0.88 (0.75-1.04) | 0.05 |
| Hypertriglyceridemia | | | | |
| Cases, n (%) | 1070 (15.4) | 920 (14.7) | 1505 (20.9) | |
| Age and sex adjusted | 1.0 | 0.95(0.79-1.13) | 1.45(1.21-1.73) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.02(0.85-1.23) | 0.96(0.78-1.19) | 0.58 |
| +BMI adjusted | 1.0 | 0.8(0.66-0.97) | 0.82(0.66-1.01) | 0.84 |
| Low HDL cholesterol | | | | |
| Cases, n (%) | 2120 (26.9) | 2294 (38.8) | 2624 (34.5) | |
| Age and sex adjusted | 1.0 | 1.69(1.47-1.96) | 1.45(1.24-1.68) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.68(1.44-1.95) | 1.41(1.19-1.67) | 0.046 |
| +BMI adjusted | 1.0 | 1.46(1.25-1.70) | 1.26(1.05-1.50) | 0.09 |
| Hyperglycemia | | | | |
| Cases, n (%) | 753 (8.7) | 663 (10.2) | 1452 (18.3) | |
| Age and sex adjusted | 1.0 | 1.17(0.97-1.41) | 2.37(1.98-2.84) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.14(0.95-1.37) | 1.64(1.31-2.04) | 0.0006 |
| +BMI adjusted | 1.0 | 0.97(0.80-1.18) | 1.47(1.18-1.84) | <0.0001 |
| Central obesity | | | | |
| Cases, n (%) | 2119 (27.0) | 2232 (38.9) | 4146 (53.7) | |
| Age and sex adjusted | 1.0 | 1.69(1.47-1.93) | 3.14(2.73-3.60) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.95(1.70-2.24) | 2.06(1.74-2.42) | 0.49 |
| +BMI adjusted | 1.0 | 1.30(1.06-1.60) | 1.71(1.36-2.16) | 0.02 |
| Number of MS components | | | | |
| One or more | | | | |
| Cases, n (%) | 5191 (69.2) | 4532 (78.0) | 6399 (84.0) | |
| Age and sex adjusted | 1.0 | 1.53(1.30-1.79) | 2.35(2.00-2.76) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.64(1.38-1.95) | 1.70(1.43-2.01) | 0.73 |
| +BMI adjusted | 1.0 | 1.23(1.01-1.49) | 1.29(1.06-1.57) | 0.64 |
| Two or more | | | | |
| Cases, n (%) | 2687 (34.7) | 2754 (46.8) | 4329 (56.2) | |
| Age and sex adjusted | 1.0 | 1.61(1.41-1.84) | 2.44(2.14-2.79) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.75(1.52-2.01) | 1.67(1.43-1.95) | 0.56 |
| +BMI adjusted | 1.0 | 1.22(1.04-1.44) | 1.26(1.04-1.53) | 0.75 |
| Four or more | | | | |
| Cases, n (%) | 368 (5.1) | 414 (6.6) | 816 (11.1) | |
| Age and sex adjusted | 1.0 | 1.28(0.99-1.67) | 2.33(1.81-3.0) | <0.0001 |
| Multivariable adjusted[a] | 1.0 | 1.35(1.02-1.77) | 1.44(1.05-1.98) | 0.64 |
| +BMI adjusted | 1.0 | 0.90(0.66-1.24) | 1.16(0.84-1.61) | 0.11 |

*P<0.05 for comparison between participants of the 'Yellow Earth' dietary pattern and participants of the 'Western/new affluence' dietary pattern using Survey logistic model by treating 'Western/new affluence' dietary pattern as reference.

[a]Adjusted for age(continue), sex, family income(<2000,2000-4999,≥5000 RMB/person/year), living area(urban/rural), current smoking(yes/no), drinking(yes/no), physical activity level(light, low active, very active), education level(illiterate, primary, high school, above high school), cooking salt(continue) and salted vegetable(continue) consumption, dietary energy intakes(continue), family history of hypertension(yes/no) and history of diabetes(yes/no).

**Table 5.4** Stratified analysis of the association between dietary patterns and MS

| | | 'Green Water' | 'Yellow Earth' | 'Western/new affluence' |
|---|---|---|---|---|
| Sex | Male (n=9936) | 1.0 | 1.20(0.91-1.58) | 1.17(0.86-1.60) |
| | Female (n=10891) | 1.0 | 1.97(1.59-2.44) | 1.53(1.19-1.97) |
| Age | 45~54 yrs (n=11171) | 1.0 | 1.59(1.26-2.02) | 1.35(1.02-1.80) |
| | 55~69 yrs (n=9656) | 1.0 | 1.71(1.36-2.15) | 1.37(1.06-1.79) |
| Area | Rural (n=12984) | 1.0 | 1.81(1.52-2.16) | 1.84(1.47-2.32) |
| | City (n=7843) | 1.0 | 1.41(0.96-2.09) | 1.08(0.8-1.45) |
| Current smoker | Absence (n=14636) | 1.0 | 1.85(1.53-2.24) | 1.51(1.21-1.88) |
| | Presence (N=6191) | 1.0 | 1.07(0.77-1.48) | 1.01(0.68-1.51) |
| Drinking | No (n=15884) | 1.0 | 1.80(1.49-2.17) | 1.51(1.21-1.88) |
| | Yes (n=4943) | 1.0 | 1.05(0.72-1.54) | 1.03(0.68-1.56) |
| Physical activity level | Sedentary (n=5900) | 1.0 | 1.80(1.31-2.48) | 1.23(0.88-1.73) |
| | Low active (n=4276) | 1.0 | 1.45(0.98-2.14) | 1.13(0.77-1.66) |
| | Active (n=3342) | 1.0 | 1.23(0.82-1.76) | 1.19(0.76-1.86) |
| | Very active (n=7309) | 1.0 | 1.92(1.49-2.47) | 2.40(1.70-3.38) |

Adjusted for age (continue), sex, family income (<2000, 2000-4999, ≥5000RMB/person/year), living area (urban/rural), current smoking (yes/no), drinking (yes/no), physical activity level (light, low active, active, very active), education level (Illiterate, primary, high school, above high school), cooking salt (continue) and salted vegetable (continue) consumption, dietary energy intakes (continue), family history of hypertension (yes/no) and family history of diabetes (yes/no) (stratified variable was excluded from the model).

Physical activity showed significant interactions with the dietary patterns in relation to MS risk (*P* for interaction = 0.008). Very active participants have a 60% (45-71%), 53% (40-63%) and 41% (21-56%) lower odds of MS than sedentary participants with the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern, respectively. We also examined the joint effects of dietary patterns and physical activity level in relation to MS risk (Fig. 5.1). Participants with the combination of sedentary activity with the 'Yellow Earth' dietary pattern or the 'Western/new affluence' dietary pattern both had more than three times (95% CI: 2.8-6.1) higher odds of MS than those with active activity and the 'Green Water' dietary pattern.

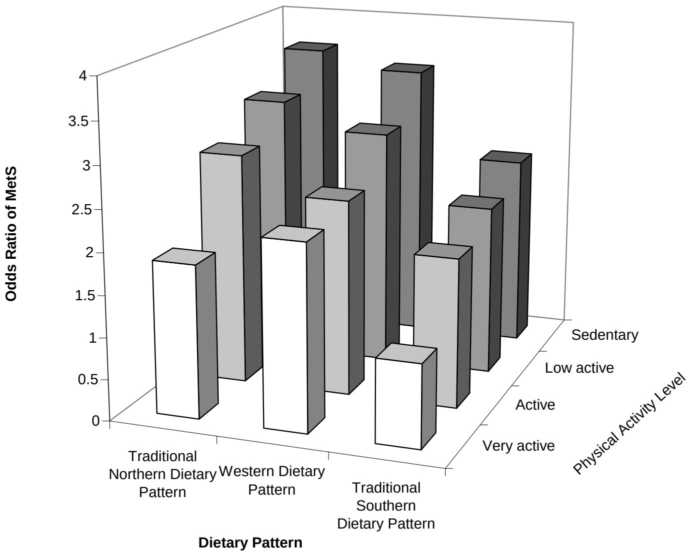


**Figure 5.1** Joint association of metabolic syndrome between dietary patterns and physical activity level. [a] Adjusted age (continue),sex, family income (<2000, 2000e4999, _5000 RMB/person/year), living area (urban/rural), current smoking (yes/no), drinking(yes/no), education level (Illiterate, primary, high school, above high school), cooking salt (continue) and salted vegetable (continue) consumption, dietary energy intakes (continue), family history of hypertension (yes/no) and family history of diabetes (yes/no).

## Discussion

Using data from the nationally-representative sample of Chinese adults, we featured three habitual dietary patterns: the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern. The 'Green Water' dietary pattern, characterized by high intakes of rice and vegetables and moderate intakes of animal foods, was associated with the lowest prevalence of MS and its individual components. As compared with the 'Green Water' dietary pattern, the 'Yellow Earth' dietary pattern characterized by high intakes of cereal products, tubers and salted vegetable and the 'Western/new affluence' dietary pattern characterized by high intakes of beef/lamb, fruit, eggs, poultry and seafood were associated with elevated likelihood of MS and its components.

The 'Yellow Earth' dietary pattern was a typical traditional dietary pattern in North China, while the 'Green Water' dietary pattern was a typical traditional pattern in South China. The prevalence of abdominal obesity, hypertriglyceridemia, low HDL, high fasting glucose and overweight (20), as well as stroke (21), had been reported higher in northern compared to southern China. It was previously reported that the north–south differences in MS components such as blood pressure might be explained by the dietary factors (22). Our data lend strong support to that dietary patterns may account for the north–south differences in MS. Refined carbohydrate foods and sodium (23) from cooking salt and salted vegetables, which are high in the 'Yellow Earth' dietary patterns, may contribute to the high risk of MS; while intakes of vegetables, which are high in the 'Green Water' dietary pattern, may partly account for the low risk of MS. Our recent paper also reported significant association between the traditional 'Yellow Earth' dietary pattern and stroke (24).

Consistent with our findings, a 'Western/new affluence' dietary pattern was associated with MS in Americans, Mexicans and Iran women (2-5). Also consistent with ours are the previous findings about the MS and its components were associated with high intakes of beef, lamb, poultry and eggs (25, 26), which are all important components of the 'Western/new affluence' dietary pattern. The associations between dietary patterns and MS attenuated after controlling for BMI. The results indicate that the associations between dietary patterns and MS risk may be partially mediated through the dietary effects on overall obesity. The significant protective association between the 'Yellow Earth' dietary patterns and hypertriglyceridemia we observed in the final model is more likely due to the over adjustment of BMI. Association between dietary pattern and hypertriglyceridemia in Chinese population still warrants further studies.

We found significant physical activity-dietary patterns interaction in relation to MS. Low physical activity level showed additive effects with the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern on MS risk. Physical inactivity has been previously related to MS in various ethnic and socioeconomic groups (27, 28). The data from the present study suggest that individuals with healthy dietary pattern (Green Water) and taking active lifestyle may benefit more in prevention of MS. Our observation was supported by the clinical trials in which a combination of diet and exercise intervention showed more effective than either approach alone in reduction of MS (29, 30).

The present study is thus far the largest study in China with nationally-representative data of dietary intakes and MS. Based on this data, we were able to identify the nation-wide eating patterns of Chinese adults during nutrition transition and examine their joint effects with physical activity on likelihood of MS. However, a cross-sectional design disallows a sequence of temporality to be established for MS and dietary patterns. In order to minimize this limitation, we did a sensitivity analysis by excluding participants who were aware of their metabolic aberrations, including diabetes, hypertension or dyslipidemia. The results from the sensitivity analyses were highly consistent with those obtained from the whole study population. Another limitation of present study is the lack of validation study of our physical activity questionnaire. Future prospective cohort studies based on validated physical activity measurements are warranted to further verify our findings.

In conclusion, in the large-scale, nationally-representive sample of Chinese adults, we found that the 'Yellow Earth' dietary pattern and the 'Western/new affluence' dietary pattern are associated with an increased likelihood of MS as compared with the 'Green Water' dietary pattern. For the first time, we demonstrated an additive effect of physical activity and dietary patterns in relation to high odds of MS.

## Author contribution

Y.L. had full access to all of the data in the study, analyzed the data, contributed to the discussion, interpretation of the data, and the manuscript writing, and takes responsibility for the integrity of the data and the accuracy of the data analysis. Y.H. had full access to all of the data in the study, analyzed the data, contributed to the discussion, interpretation of the data, and the manuscript writing. X.Y., J.L., J.Z. and P.F. were the principal investigators of the 2002 CNNHS, contributed to the discussion, interpretation of the data, and the manuscript writing. D.W. contributed to the analysis, interpretation of the data, the discussion, and the writing of the manuscript. L.Q. contributed to the study design, discussion, interpretation of the data, and manuscript writing.

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## Appendix A. Supplementary material

Supplementary material related to this article can be found online at http://dx.doi.org/10.1016/j.numecd.2012.09.001.

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# CHAPTER 6

## Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood

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## Abstract

**Objective:** Early developmental adaptations in response to undernutrition may play an essential role in susceptibility to type 2 diabetes, particularly for those experiencing a "mismatched rich nutritional environment" in later life. We examined the associations of exposure to the Chinese famine (1959-1961) during fetal life and childhood with the risk of hyperglycemia and type 2 diabetes in adulthood.

**Research Design and Methods:** We used the data of 7,874 rural adults born between 1954 and 1964 in the selected communities from the cross-sectional 2002 China National Nutrition and Health Survey. Hyperglycemia was defined as fasting plasma glucose ≥6.1mmol/L and/or 2-h plasma glucose ≥7.8 mmol/L and/or a previous clinical diagnosed of type 2 diabetes.

**Results:** Prevalences of hyperglycemia among adults in nonexposed, fetal exposed, early-childhood, mid-childhood and late-childhood exposed cohorts were 2.4%, 5.7%, 3.9%, 3.4% and 5.9%, respectively. In severely affected famine areas, fetal-exposed subjects had an increased risk of hyperglycemia compared with nonexposed subjects (Odds ratio=3.92; 95%CI: 1.64-9.39; *P*=0.002); this difference was not observed in less severely affected famine areas (Odds ratio=0.57; 95%CI: 0.25-1.31; *P*=0.185); The odds ratios were significantly different between groups from the severe and less severe famine areas (*P for interaction* =0.001). In severely affected famine areas, fetal-exposed subjects who followed an affluent/western dietary pattern (Odds ratios=7.63; 95%CI: 2.41-24.1; *P*=0.0005) or who had a higher economic status in later life experienced a substantially elevated risk of hyperglycemia (Odds ratios=6.20; 95%CI: 2.08-18.5; *P*=0.001).

**Conclusions:** Fetal exposure to severe Chinese famine increases the risk of hyperglycemia in adulthood. This association appears to be exacerbated by a nutritional 'rich' environment in later life.

## Introduction

The developmental origins hypothesis postulates that adaptations in response to fetal undernutrition lead to metabolic and structural changes, which are beneficial for early survival but may increase the risk of common diseases such as type 2 diabetes in adulthood (1, 2). The risks of adverse long-term consequences are further increased in a nutritionally rich environment in later life (1, 2). Indirect support for this hypothesis comes from studies showing consistent associations of low birth weight with increased risks of type 2 diabetes (2, 3). Because of ethical and practical reasons, direct evidence connecting fetal malnutrition and later diabetes risk in humans is sparse. Famine periods provide unique opportunities to investigate these relationships. Ravelli et al (4) and de Rooij et al. (5) showed that adults who had been exposed to the Dutch famine during World War II had higher insulin resistance measures than those who had not been exposed. However, this association was not observed in another famine cohort study, the Leningrad siege study (6). These inconsistent results may be caused by differences in postnatal environmental life exposures. Although the Dutch population rapidly developed into a wealthy and rich population after the famine, the Leningrad cohort remained relatively poor.

The Chinese famine lasted from the late 1950s to the early 1960s and caused millions of excess deaths (7). It was more devastating in rural areas. The most severe period with the highest mortality rate was between 1959 and 1961 (8). Fetal exposure to the Chinese famine has been associated with the risks of overweight and schizophrenia in adult life (7, 9-12). However, no study has examined the Chinese famine effects in early life on the risk of abnormalities in glucose metabolism and diabetes.

We used data from the 2002 China National Nutrition and Health Survey (CNNHS) to examine the associations between famine exposure in fetal life and childhood with risks of hyperglycemia and type 2 diabetes in adulthood, and to examine whether a nutritional rich environment in later life modifies these associations.

## Research Design and Methods

The 2002 CNNHS is a nationally representative cross-sectional study on nutrition and chronic diseases. A stratified, multistage probability cluster sampling design was used in this survey(13). Based on socioeconomic characteristics, the country was divided into six regions. As shown in **Fig 6.1**, in the first stage of sampling, 22 counties were randomly selected from each of the 6 regions in China. In the second stage, three townships were randomly selected from each of the selected counties. From each of the townships, 2 residential villages were randomly selected; and 90 households were then randomly sampled from each village for physical examination. One-third of the households were selected to participate in the dietary survey and blood draw. For the present study, we used residents who were living in rural area and were born between October 1, 1952 and September 30, 1964 as our analytic population. To minimize misclassification of the exposure periods, subjects who were born between October 1, 1958 and September 30, 1959 and between October 1, 1961 and September 30, 1962 were excluded since the exact dates of the start and the end of the Chinese famine were not available and not the same across regions. Our total sample size was 7,874 people.

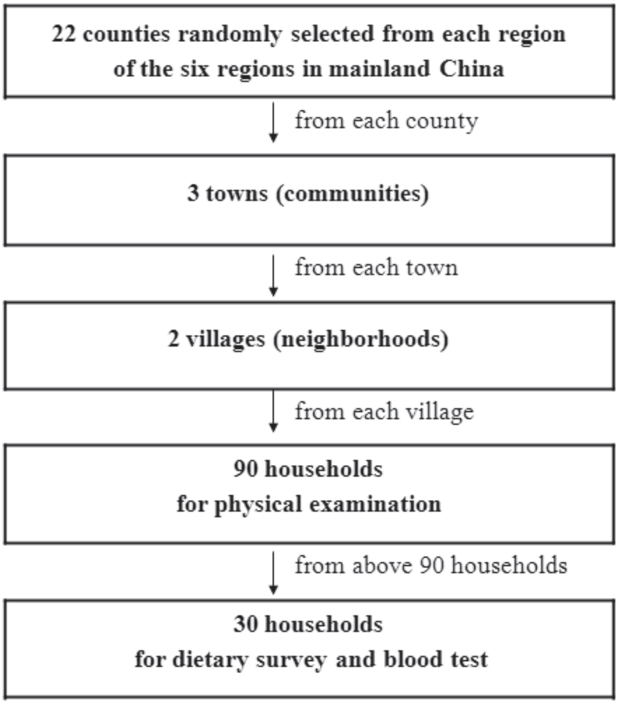


**Figure 6.1**. Flow chart on the sampling method in each region* of 2002 China National Nutrition and Health Survey. *The mainland of China is classified into 6 regions defined by Chinese Bureau of Statistics according to their socioeconomic development. They are metropolis, general city, type I rural site, type II rural site, type III rural site, and type IV rural site.

*Famine cohorts and areas*

Subjects were categorized into five exposure cohorts: non-exposed cohort, fetal-exposed cohort, early childhood-exposed cohort, mid childhood-exposed cohort and late childhood-exposed cohort. All cohorts were defined according to the subjects' birth dates. Subjects who were born between October 1, 1962 and September 30, 1964 were classified as the nonexposed cohort; and subjects who were born between October 1, 1959 and September 30, 1961, were classified as fetal-exposed cohort. Subjects who were born between October 1, 1952, and September 30, 1958, were grouped by every 2 years and were classified into one of the three childhood-exposed cohorts. Mean ages for subjects in nonexposed cohort, fetal-exposed cohort, early childhood-exposed cohort, mid childhood-exposed cohort and late childhood-exposed cohort was 39, 42, 45, 47 and 49 years, respectively.

The Chinese famine affected the entire mainland of China, but the severity varied across regions due to different weather conditions, population density, and local policies regarding food shortage (7). As previously described, we used the excess death rate of each province to determine the severity of the famine(7). The excess death rate was calculated as the percentage change in mortality rate from the mean level in 1956-1958 to the highest value during the period of 1959-1961 (7). An excess death rate of 50% was used as the threshold: regions that had an equal or higher rate than this cutoff were categorized as severely affected famine areas, and otherwise as less severely affected famine areas. We split all five cohorts into severely affected famine areas and less severely affected famine areas. This enabled us to test the hypothesis that the famine effect is stronger in the severely affected famine areas than that in the less severely affected famine areas and to consider both birth cohort effects and regional differences.

*Assessments of blood glucose and type 2 diabetes*

All subjects were invited for blood collection after an 10 to 14 h overnight fast. The plasma was separated by centrifugation at 3200 rpm for 10-15 min within 1 h of collection, and kept at room temperature without sunshine. Fasting plasma glucose (FPG) concentration was measured using glucose oxidize enzymatic method within 3 h of plasma preparation. Every tenth sample was measured twice (the correlation coefficient of duplicate measurements was 0.98). All individuals had fasting glucose levels measured. A 75-g oral glucose tolerance test was performed in subjects whose FPG was ≥5.5 mmol/L. We used criteria proposed by the WHO Expert Committee on Diabetes Mellitus(14). Type 2 diabetes was defined as FPG ≥7 mmol/L and/or 2-h plasma glucose ≥11.1 mmol/L. Hyperglycemia was defined as FPG ≥6.1mmol/L and/or 2-h plasma glucose ≥7.8

mmol/L, including impaired fasting glucose, impaired glucose tolerance, and type 2 diabetes. In addition, subjects who have been previously diagnosed with type 2 diabetes were added as cases of hyperglycemia and type 2 diabetes.

*Stratification factors*

Dietary patterns, economic status and BMI measured in 2002 were used as measures of the nutritional environment in adulthood and to examine the "mismatch" between fetal nutrition and adult nutrition.

The method for assessing dietary patterns has been described in detail elsewhere(15). Briefly, four dietary patterns were derived through cluster analysis, which were labeled as "green water", "yellow earth", "new affluence", and "western adopter". "Green water" and "yellow earth" patterns represent the traditional Chinese diets in South and the North, respectively, whereas the other two represent Westernized dietary patterns. In this study, we combined the clusters of "green water" and "yellow earth" as the traditional dietary pattern, and we combined the clusters of "new affluence" and "Western adopter" as the affluent/western pattern.

Current economic status was assessed by the mean annual income in the year prior to the 2002 CNNHS, which was treated as a dichotomous variable. The mean level of the current sample (2000 Chinese Yuan per person per year) was used as a cutoff point for economic status.

BMI was calculated by measured height and fasting body weight. We used the criteria recommended for Chinese adults and classified subjects as overweight if BMI $\geq$ 24 kg/$m^2$, or otherwise normal (16).

The protocol of the 2002 CNNHS was approved by the Ethical Committee of the National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. Signed consent forms were obtained from all participants.

*Statistical analyses.*

We performed survey analyses in SAS 9.2 for Windows (SAS Institute , Cary, NC) to estimate statistics for this complex, multistage-designed survey sample. Survey weights were derived from the 2000 China National Population Census and associated administrative data. The population of 2000 China National Population Census was also used for sex standardization.

Mean FPG differences between the exposed cohorts and the nonexposed cohort were tested by generalized least squares estimation (17). Risks of hyperglycemia and type 2 diabetes among fetal and childhood-exposed subjects, compared with nonexposed subjects, were examined with the method of maximum likelihood by using survey logistic regression model. Interaction between famine exposure cohort (fetal- or childhood-exposed vs. non-exposed) and area (severely affected and less severely affected) was tested by adding a multiplicative factor in the survey logistic regression model. Analyses were adjusted for sex, family history of diabetes, educational level, current smoking, alcohol use and physical activity level, all assessed in 2002.

To explore whether the associations between fetal exposure to severe famine and hyperglycemia were affected by an improved nutritional environment in later life, we subsequently stratified the analyses by dietary patterns, economic status and BMI in adulthood. Prevalence of hyperglycemia was plotted according to cohort and classification of the stratification factors. The odds ratio of hyperglycemia in the fetal-exposed cohort compared with the nonexposed cohort was calculated within each category of the stratified factor.

To distinguish severely and less severely affected famine areas more appropriately, we performed sensitivity analysis by using a more stringent cutoff point, i.e. we used an excess death rate ≥100% to define the severity of famine. In addition, we performed analyses by using the cohort born during October 1, 1962, to September 30, 1968, as a nonexposed cohort for association analyses, or by excluding participants with a family history of diabetes.

## Results

Basic characteristics of the study population are shown in Table 6.1. In our main study population (n=7874), 1005 (12.8%) subjects had been exposed to the Chinese famine during fetal life, and 4915 (62.4%) subjects had been exposed during childhood. As compared with the nonexposed individuals, fetal-exposed subjects were 0.9 cm shorter as adults, and childhood-exposed subjects were 1.5 cm shorter **(Table 1).** The prevalence of hyperglycemia among adults in nonexposed, fetal-exposed, early childhood-, mid childhood-, and late childhood-exposed birth cohort was 2.4%, 5.7%, 3.9%, 3.4% and 5.9%, respectively.

In severely affected famine areas, FPG concentration was significantly higher in the fetal-exposed cohort than in the nonexposed cohort with a mean difference of 0.20mmol/L (95%CI: 0.06-0.35, *P*=0.007). No significant difference was observed in the less severely affected famine areas (*P for interaction*=0.001, **Table 6.2**). Compared with nonexposed subjects, FPG was higher in late childhood-exposed cohort in both the severely affected famine areas and less severely affected famine areas. Differences were not significant for the early and mid childhood-exposed cohorts. A significant interaction between the exposed cohort and areas was found only for the fetal-exposed cohort **(Table 6.2)**.

**Table 6.1** Basic characteristics of study population according to Chinese famine exposure

| | Childhood exposed cohorts | | | Fetal-exposed Cohort | Non-exposed Cohort |
|---|---|---|---|---|---|
| | Late-child | Mid-child | Early-child | | |
| N | 1673 | 1588 | 1654 | 1005 | 1954 |
| Severe affected area | 896 | 888 | 940 | 503 | 1132 |
| Less severe affected area | 777 | 700 | 714 | 502 | 822 |
| Birth Day | | | | | |
| (from October 1, Year) | 1952 | 1954 | 1956 | 1959 | 1962 |
| (To September 30, Year) | 1954 | 1956 | 1958 | 1961 | 1964 |
| Age in 2002 (years) | 48-49 | 46-47 | 44-45 | 41-42 | 38-39 |
| Women (%) | 54.0 | 54.2 | 54.0 | 53.2 | 55.5 |
| Height (cm)[*] | 159.3 (0.2)[†] | 159.4 (0.4)[†] | 159.4 (0.2)[†] | 160.0 (0.4)[†] | 160.9 (0.2) |
| Weight (kg)[**] | 59.4 (0.4) | 58.9 (0.5) | 59.0 (0.5) | 59.6 (0.5) | 59.2 (0.3) |
| Body mass index ($kg/m^2$)[**] | 23.3 (0.1)[†] | 23.1 (0.2) | 23.2 (0.2) | 23.2 (0.2) | 22.9 (0.1) |
| Fasting plasma glucose (mmol/L)[**] | 4.99 (0.05)[†] | 4.88 (0.04)[†] | 4.87 (0.04)[†] | 4.88 (0.05)[†] | 4.77 (0.03) |
| Hyperglycemia (%)[*] | 5.89[†] | 3.40 | 3.93 | 5.65[†] | 2.43 |
| Type 2 diabetes (%)[*] | 3.89[†] | 1.69 | 2.78 | 1.70 | 1.57 |

[*] Sex standard. **Data are adjusted means (SE). Adjusted factors included sex, educational level, family history of diabetes (only for glucose), current smoking, alcohol use, and physical activity level. Height was only adjusted for sex.[†] Compared to the non-exposed cohort, [†]*P*<0.05

Subjects exposed to famine during fetal life in severely affected famine areas had a higher prevalence of hyperglycemia than the nonexposed cohort. This difference was not significant in the less severely affected famine areas. The odds ratios were significantly different between the severe and less severe famine areas **(Table 6.2),** suggesting a stronger famine effect in the severely affected famine areas. Compared with the nonexposed cohort, subjects in late childhood-exposed cohort had a higher risk of hyperglycemia in both severely and less severely affected famine areas, but the odds ratios were not significantly different between the severe and less severe famine areas **(Table 6.2)**.

A significantly higher prevalence of type 2 diabetes was observed among subjects exposed in late childhood as compared with the nonexposed cohort (Table 1). However, Table 2 shows that after stratification of this group by severity of famine exposure, no significant difference of type 2 diabetes risk was observed anymore between different famine cohorts.

Stratified analyses by dietary pattern, economic status and BMI for severely affected famine areas are shown in **Fig.6.2. Figure 6.2A1** shows that the prevalence of hyperglycemia was the highest (18.9%) in subjects in the fetal-exposed cohort and who consumed an affluent/western diet. As compared with the relatively nonexposed cohort, the odds ratio of hyperglycemia in the fetal-exposed cohort was 7.63 (95%CI:

2.41-24.1, *P*=0.0005) for those who had an affluent/Western dietary pattern, and 2.34 (95%CI: 0.82-6.70, *P*=0.112) for those with a traditional dietary pattern.

**Table 6.2** Concentrations of fasting plasma glucose and prevalence rates of hyperglycemia and type 2 diabetes by birth cohort and severity of Chinese famine area*

| | Childhood exposed cohorts* | | | Fetal exposed | Non-exposed |
|---|---|---|---|---|---|
| | Late-childhood | Mid-childhood | Early-childhood | Cohort | Cohort |
| **FASTING PLASMA GLUCOSE (FPG)** | | | | | |
| Severely affected famine area | | | | | |
| Mean (SE, mmol/L) | 4.95 (0.07) | 4.84 (0.04) | 4.87 (0.05) | 4.95 (0.07) | 4.75 (0.03) |
| *P* | 0.008 | 0.059 | 0.037 | 0.007 | Ref. |
| Less severely affected famine area | | | | | |
| Mean (SE, mmol/L) | 5.09 (0.09) | 4.97 (0.08) | 4.88 (0.04) | 4.73 (0.04) | 4.81 (0.05) |
| *P* | 0.011 | 0.113 | 0.321 | 0.234 | Ref. |
| *P* for interaction between area and cohort | 0.898 | 0.793 | 0.271 | <.0001 | |
| **HYPERGLYCEMIA** | | | | | |
| Severely affected famine area | | | | | |
| Prevalence (%) | 5.19 | 2.68 | 3.76 | 7.29 | 2.02 |
| Odds Ratio (95%CI) | 2.38 (1.11-5.11) | 1.21 (0.57-2.55) | 1.77 (0.82-3.83) | 3.92 (1.64-9.39) | Ref. |
| Less severely affected famine area | | | | | |
| Prevalence (%) | 7.17 | 5.22 | 4.34 | 2.14 | 3.46 |
| Odds Ratio (95%CI) | 2.27 (1.02-5.06) | 1.94 (0.80-4.72) | 1.16 (0.56-2.40) | 0.57 (0.25-1.31) | Ref. |
| *P* for interaction between area and cohort | 0.542 | 0.766 | 0.341 | 0.001 | |
| **TYPE 2 DIABETES** | | | | | |
| Severely affected famine area | | | | | |
| Prevalence (%) | 3.51 | 1.19 | 2.90 | 2.01 | 1.37 |
| Odds Ratio (95%CI) | 2.51 (0.91-6.87) | 0.75 (0.26-2.12) | 2.07 (0.82-5.24) | 1.43 (0.53-3.87) | Ref. |
| Less severely affected famine area | | | | | |
| Prevalence (%) | 4.60 | 2.99 | 2.48 | 1.08 | 2.08 |
| Odds Ratio (95%CI) | 2.34 (0.72-7.62) | 1.86 (0.53-6.45) | 1.02 (0.35-2.93) | 0.41 (0.12-1.35) | Ref. |
| *P* for interaction between area and cohort | 0.606 | 0.424 | 0.243 | 0.102 | |

*Data are adjusted means (SE) for FPG, and sex standard prevalence and odds ratio for hyperglycemia and diabetes. All odds ratios use nonexposed cohort as reference cohort. Adjusted factors included sex, educational level, family history of diabetes, and current smoking, alcohol use and physical activity level

**Figure 6.2A2** shows that as compared with nonexposed subjects, the odds ratio of hyperglycemia in the fetal-exposed cohort was 6.20 (95%CI: 2.08-18.5, *P*=0.001) in subjects with a higher adult economic status, and 1.68 (95%CI: 0.50-5.71, *P*=0.404) in subjects with a lower adult economic status. **Figure 6.2A3** shows that overweight subjects in the fetal-exposed cohort had the highest prevalence of hyperglycemia (13.9%). However, the risks of hyperglycemia were largely comparable in these two groups; the odds ratio of hyperglycemia in the fetal-exposed cohort was 3.71 (95%CI 1.13-12.2, *P*=0.031) in overweight subjects and 4.37 (95% CI 1.15-16.5, *P*=0.030) in normal weight subjects, respectively, compared with the nonexposed cohort. Similar analyses were performed in subjects exposed to less severely affected famine areas during fetal life and childhood (**Fig. 6.2**, right column, graphs B1, B2 and B3), but did not show consistent associations.

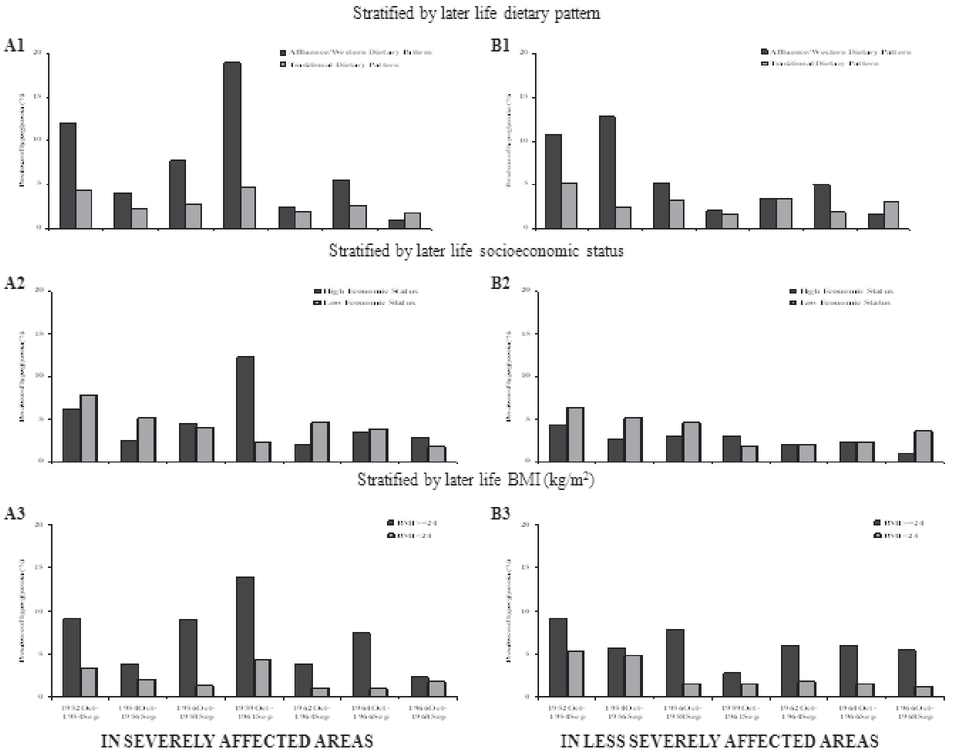


**Figure 6.2.** Prevalence of hyperglycemia among birth cohorts according to early life famine exposure and later life dietary patterns (A1 and B1), socioeconomic status (A2 and B2), and body mass index (A3 and B3) in severely (column A) and less severely affected famine areas (Column B)

When we defined the severely affected famine areas as those with an excess death rate ≥100%, the prevalence of hyperglycemia among the fetal-exposed cohort in severely affected famine areas increased to 8.1%, but this did not change the associations between fetal exposure to famine and risk of hyperglycemia in adulthood. In addition, neither using subjects who were born between October 1, 1962, and September 30, 1968, as a nonexposed cohort nor excluding subjects with a family history of diabetes materially changed the associations **(Table 6.3)**.

**Table 6.3** Prevalence rate of hyperglycaemia by birth cohorts and severity of famine areas: sensitivity analyses

| | Childhood exposed cohorts | | | Fetal exposed | Non-exposed |
|---|---|---|---|---|---|
| | Late-childhood | Mid-childhood | Early-childhood | Cohort | Cohort |
| **Defining severity of famine by excess death rate ≥100%** | | | | | |
| Severely affected famine area | | | | | |
| Prevalence (%) | 3.92 | 2.56 | 2.60 | 8.11 | 1.39 |
| Odds Ratio (95%CI) | 2.15 (0.90-5.14) | 1.56 (0.62-3.88) | 1.80 (0.66-4.92) | 6.28 (2.16-18.3) | |
| Less severely affected famine area | | | | | |
| Prevalence (%) | 7.92 | 4.42 | 5.32 | 3.39 | 3.74 |
| Odds Ratio (95%CI) | 2.54 (1.24-5.20) | 1.33 (0.62-2.88) | 1.40 (0.68-2.88) | 0.89 (0.42-1.90) | |
| *P* for interaction between area and cohort | 0.492 | 0.373 | 0.362 | 0.003 | |
| **Classifying adults born during October 1, 1962 to September 30, 1968 as non-exposed cohort** | | | | | |
| Severely affected famine area | | | | | |
| Prevalence (%) | 5.19 | 2.68 | 3.76 | 7.29 | 3.11 |
| Odds Ratio (95%CI) | 2.18 (1.21-3.93) | 1.10 (0.59-2.03) | 1.51 (0.79-2.87) | 3.38 (1.55-7.36) | |
| Less severely affected famine area | | | | | |
| Prevalence (%) | 7.17 | 5.22 | 4.34 | 2.14 | 2.33 |
| Odds Ratio (95%CI) | 2.47 (1.34-4.53) | 1.83 (0.86-3.91) | 1.30 (0.74-2.30) | 0.61 (0.30-1.26) | |
| *P* for interaction between area and cohort | 0.966 | 0.395 | 0.693 | 0.001 | |
| **Excluding people with family history of diabetes** | | | | | |
| Severely affected famine area | | | | | |
| Prevalence (%) | 5.06 | 2.64 | 3.51 | 7.08 | 1.98 |
| Odds Ratio (95%CI) | 2.40 (1.10-5.22) | 1.23 (0.57-2.63) | 1.73 (0.78-3.86) | 4.00 (1.64-9.73) | |
| Less severely affected famine area | | | | | |
| Prevalence (%) | 6.03 | 5.02 | 3.93 | 2.16 | 3.10 |
| Odds Ratio (95%CI) | 2.41 (1.00-5.81) | 1.83 (0.71-4.70) | 1.30 (0.61-2.77) | 0.67 (0.29-1.56) | |
| *P* for interaction between area and cohort | 0.505 | 0.826 | 0.488 | 0.003 | |

All odds ratios used the nonexposed cohort as reference cohort. Adjusted factors included sex, educational level, family history of diabetes, current smoking, alcohol use, and physical activity level in 2002.

## Discussion

In this study of a large sample of Chinese adults, we found a significant association between severe famine exposure during the fetal period and an increased risk of hyperglycemia in adulthood. This association was stronger in subjects with a Western dietary pattern or higher economic status in adulthood. No consistent association was observed between famine exposure during childhood and hyperglycemia.

Several mechanisms might explain the associations between fetal famine exposure and risk of diabetes in later life. Exposure to extreme starvation in rats led to poor development of pancreatic ß–cell mass and function and insulin resistance, which might persist in later life (17). A poor intrauterine environment may also reduce skeletal muscle development (18), which may subsequently lead to insulin resistance in peripheral tissues (19). It has also been suggested that stress suffering from fetal famine exposure could change the set point of the hypothalamic-pituitary-adrenal (HPA) axis, which could result in long-term changes in secretion of neuroendocrine mediators of the stress response, and predispose to cardiovascular and metabolic disease in later life (20, 21).

To our knowledge, thus far three studies have assessed the associations of exposure to the famine with measures of glucose intolerance. These studies were performed in the Netherlands (Dutch Famine Study) (4, 5), Russia (Leningrad Siege Study) (6), and China (our Chinese Famine Study). The Dutch Famine Study reported higher 2-h glucose and insulin levels among subjects who were exposed to the famine during fetal life (4, 5), but this association was not observed in the Leningrad Siege Study (6).The inconsistent results might be due to differences in postnatal environmental life exposures. Although the Dutch population rapidly developed into a wealthy and rich population after the famine, the Leningrad people remained relatively poor. In our study, we observed that fetal exposure to the severe Chinese famine increases the risk of hyperglycemia in adulthood, which was exacerbated by an unhealthy adult diet and higher economic status. Our results support the hypothesis that exposure to a nutritional rich environment modifies the association between fetal famine exposure and disease in later life (1, 19, 22).

The association between fetal famine exposure and hyperglycemia was stronger in participants with an affluent/Western dietary pattern. These subjects were, to a large extent, less poor and more highly educated (15), and they have benefited most from the dramatically enhanced economic opportunities and have broken away from the traditional Chinese food patterns (15). Their diet is characterized by a high intake of meat, eggs, dairy, sugary beverages, edible oils and a low vegetable use (15). Apparently, this nutrition “rich” environment did not match the fetal starvation environment that people of fetal exposed cohort experienced, which in turn increased the risk of hyperglycemia in later life (1, 19, 22).

Our study used annual mean income as the cutoff to categorize the economic status (2000 Chinese Yuan/Person/Year). Subjects in the lower economic group might consume mostly traditional plant foods with little meat. Therefore, the discrepancy between the nutritional environment in adulthood and fetal under-nutrition conditions may be less evident for those with a higher economic status. In other words, there was probably greater ‘mismatch’ between in utero and adulthood environments in the higher economic group, which triggered an increased prevalence of hyperglycemia in the fetal-exposed cohort.

Overweight may also represent a nutritional “rich” environment. Overweight subjects in the fetal-exposed cohort had the highest prevalence of hyperglycemia. Similar results were described in the Dutch famine study (4) showing that the 2-h glucose concentrations were especially high among people exposed to the famine during fetal life and who became obese in later life. However, the relative risk of hyperglycemia in overweight subjects was not different from that in normal weight subjects. This may be partly due to the increased prevalence of hyperglycemia in the non-exposed cohort in overweight subset. These results therefore indicate that both improving fetal nutritional environmental and controlling BMI in later life are important for prevention of a disturbed glucose metabolism.

Childhood nutritional status, particularly during infancy, is another key factor in influencing the propensity to develop disease in adulthood (22). Animal studies showed that postnatal caloric restriction might hamper β-cell development(23)and might disturb glucose metabolism in later life in rats (24). Our study found significantly increased FPG in the early childhood-exposed cohort in the severely affected famine areas, but no significant differences in FPG in the less severely affected famine areas. We also observed a higher risk of hyperglycemia among subjects exposed in late childhood in both severely and less severely affected famine areas. These results suggest that famine exposure during childhood may increase the risk of hyperglycemia in later life. However, we cannot exclude a potential cohort effect, such as aging (25). Similar risks of hyperglycemia among subjects exposed during childhood in both famine-exposed areas and nonfamine-exposed areas suggest rather a cohort (older age) effect than famine effect. However, since almost all rural regions in China were affected by the famine during 1959-1961, no valid nonfamine-exposed cohort comprising subjects born in the same time period was available. Thus, the association between childhood exposure to famine and risk of hyperglycemia needs to studies in more detail.

Some limitations should be noticed. First, we assumed that the residents we investigated at the time of the survey were born in the same province and in a similar rural area. This may not be the case for all of our subjects. However, severe restrictions on migration and relocation in China made our sample quite stable. Migration with permanent resident permission still needed to be approved by authorities on a case-by-case basis in China. According to the 2000 China National Population Census, 2.68% of the rural population lived in provinces other than the provinces of their birthplaces (27). Our study sample was based on the residence registration system; only subjects with permanent resident permission in local areas were involved in our study. Therefore, we do not expect that intraprovince migration leading to measurement error in the coding of birth place is a major concern in our results(12). Second, subjects in our fetal-exposed cohort may have actually experienced severe famine during both fetal period and the infancy period because the famine lasted approximately 3 years. It was therefore difficult to distinguish whether the fetal period or the infancy period was more important. However, the early childhood cohort also included subjects exposed to famine in the infancy, which did not have a substantial influence on the risk of hyperglycemia. Thus, our results indicate that the fetal period should be considered as the primary critical period. Third, our subjects who experienced severe famine in fetal period were in their early 40s in 2002, and the cases of type 2 diabetes were few. The small numbers may partly explain why we did not observed significant associations with the risk of type 2 diabetes. We used the excess death rate as an indirect measure of famine exposure. With this method, we could not distinguish death due to famine from death due to unfavorable weather conditions or infections. We also did not have reliable information about individual food availability during the famine period. Therefore, from our data, we cannot conclude that the higher risk of hyperglycemia among subjects exposed to famine is exclusively due to malnutrition in early life. However, nutrition deficiency was highly prevalent during the Chinese famine. China’s grain output declined by 15% in 1959 and in the following 2 years, and its food supply plunged further to 70% of its 1958 level (8). As almost all foods were delivered through communal kitchens at that time, no social groups were spared from the effects of the famine (9). In addition, we did not have data on birth size and childhood growth. However, since the famine effect on glucose intolerance did not depend on birth size in the Dutch Famine Study (4), we do not consider the lack of information about individual birth outcomes as a major limitation.

In conclusion, we found that exposure to severe famine in fetal life increased the risk of hyperglycemia in adulthood. The “mismatched nutrition postnatal environment” represented by a Western dietary pattern and improved economic status further increased susceptibility to hyperglycemia in those who experienced fetal exposure to famine. Together with previous studies, our study emphasizes that early life environment is critical for the risk of hyperglycemia in adult life.

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Y.L. had full access to all of the data in the study, analyzed the data, contributed to the discussion, interpretation of the data, and the manuscript writing, and takes responsibility for the integrity of the data and the accuracy of the data analysis. Y.H. had full access to all of the data in the study, analyzed the data, contributed to the discussion, interpretation of the data, and the manuscript writing. G.M. and X.Y. were the principal investigators of the 2002 CNNHS, contributed to the discussion, interpretation of the data, and the manuscript writing. V.W.J. and L.Q. contributed to the analysis framework, interpretation of the data, the discussion, and the writing of the manuscript. E.J.M.F. contributed to the discussion and interpretation of the data. F.B.H. contributed to the discussion, interpretation of the data, and manuscript writing, and conceptualized and supervised the study

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# CHAPTER 7

## General discussion

Yuna He

This thesis has focused on the impact of lifestyle factors on the risk of type 2 diabetes in the Chinese population. This last chapter focuses on methodological matters and starts with a summary of the main findings. Thereafter, remaining issues and challenges, and the need for future improvements, are discussed in a wider perspective.

## Main findings

In 2002, the prevalence of type 2 diabetes among Chinese adults was 2.6%; an additional 1.9% had impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) (1). The prevalence was more than two-fold higher in urban than in rural residents. Body mass index (BMI), waist, and waist to height ratio (WHtR) were all strongly associated with the prevalence of glucose tolerance abnormalities. However, WHtR was a better predictor of glucose tolerance than BMI. A WHtR cut-off point of 0.5 for both men and women is suggested as optimum for predicting glucose tolerance abnormalities and may be a useful tool for screening and health education purposes **(Chapter 2)**.

**Chapters 3 and 4** present the results on the main effects of dietary factors on the subsequent prevalence of glucose tolerance abnormalities. Four dietary clusters were established after analysis of data collected via a semi-quantitative food frequency questionnaire: 'Western Adopter' (Western-like pattern), 'Green Water' (high vegetable and moderate animal food style as in the southeast area), 'New Affluence' (rich in animal and soy products such as those consumed by well-to-do individuals), and 'Yellow Earth' (high carbohydrate and low fruit, vegetable, and animal dishes, common in the northwest area). Compared to 'Green Water' consumers, the prevalence of glucose tolerance abnormalities in 'Yellow Earth' was 22% higher, and in 'New Affluence' two-fold higher **(Chapter 3)**. All participants were scored regarding their energy contribution from carbohydrates, fats, and protein to rank them in terms of a high fat–low CHO diet. After adjustment for main confounders, the prevalence ratio of type 2 diabetes in the highest quintile of the high fat/protein–low CHO diet score was 2.75. It can be concluded that high fat/protein–low CHO diets, which are quite different from the traditional Chinese diets, are associated with a higher prevalence of type 2 diabetes in China **(Chapter 4)**.

In **Chapter 5**, we examined dietary patterns and their joint effects with physical activity on the likelihood of presenting with metabolic syndrome (MS) (2). We found a significant interaction between physical activity and dietary patterns in relation to MS. A low physical activity level showed additive effects with the 'Yellow Earth' dietary pattern and the 'Western/New Affluence' dietary pattern on MS risk.

In **Chapter 6,** we examined the association of exposure to the Chinese famine (1959–1961) during fetal life or childhood with glucose tolerance abnormalities and type 2diabetes in adulthood. The prevalence of glucose tolerance abnormalities among adults in non-exposed, fetal exposed, early-childhood exposed, mid-childhood exposed, and late-childhood exposed cohorts was 2.4%, 5.7%, 3.9%, 3.4%, and5.9%, respectively. In severely affected famine areas, fetal-exposed persons had a higher risk of glucose tolerance abnormalities than non-exposed persons (OR=3.92). In severely affected famine areas, fetal-exposed subjects who followed a New Affluence/Western dietary pattern (OR=7.63), or who had a higher economic status in later life (OR=6.20), experienced a substantially elevated risk of glucose tolerance abnormalities. Fetal exposure to the severe Chinese famine increased the risk of glucose tolerance abnormalities in adulthood. This association appears to be exacerbated by a nutritionally rich environment in later life.

## Methodological issues

### *Representativeness of the study population*

The data used in **Chapters 2 to 6** were from the 2002 China National Nutrition and Health Survey (CNNHS), which is a nationally representative survey (3). In order to be nationally representative and sufficiently representative of urban and rural areas, respectively, a 4-stage stratified random sampling method with equal sample size was used.

The demographic indexes *gender ratio*, *family size*, and *proportion of minority* in the 2002 CNNHS were compared with those of the 2000 China

National Population Census (4). Differences were small and not significant. The goodness-of-fit test was used to compare the age distributions with the national population, and no significant differences were found; Myer's Index was only 4.2, indicating the absence of age-related selection (5).

There was no record of the participation rate of individuals. Among the 792 villages/neighborhood committees randomly selected, 727(91.8%) agreed to participate. In such cases, another village/neighborhood committee was randomly selected from the remaining ones. According to the investigators who carried out the measurements in 2002, once the village/neighborhood committee decided to participate, the individual response rate was always more than 90%.

On the basis of these data, we conclude that the sampling of the study population was representative of various economic development levels and types in China.

***Dietary survey***

The 23,470 households participating in the dietary assessment were randomly selected in the 2002 CNNHS. All family members (68,962 participants) in the selected households participated in the dietary survey, a 24-hour recall on 3 consecutive days including 2 weekdays and 1 weekend day. The amounts of cooking oil and condiments consumed during the 3 days were obtained using a food weighing method. In a sub-sample of 23,198 participants, information on dietary intake was also collected by weighing the food on the same days as the 24-hour recall. The interviewers were trained for both interviewing and weighing foods. The same interviewer performed the dietary recall and food weighing on the 3 survey days. Additional data analysis showed that the correlation coefficients of food intakes between food weighing and the 24-hour recall method ranged from 0.58 to 0.88. Hence we conclude that the dietary assessment in the present study is reliable and valid (6).

For the dietary pattern study, data from a semi-quantitative food frequency questionnaire (FFQ) were used to obtain information on the usual diet in the year prior to the study. In a previous study, food group consumption, energy, and nutrient intake, estimated using a FFQ, were validated against the 3 consecutive days' food-weighing method. The results showed that, using the food weighing method as the gold standard, the FFQ could accurately estimate the dietary food intake, especially for foods consumed frequently. For the less frequently consumed food items, the variety of dietary food intakes estimated by the FFQ is greater than that estimated by the food-weighing method, with a low to moderate significant correlation between the 2 methods. The main reason for this difference is probably a true difference between what was estimated; the FFQ estimates food consumption in the last year, whereas the food-weighing method estimates the food consumption in recent few days (6).

Four dietary patterns were derived by using factor analysis combined with cluster analysis. Factor analysis is widely used to reduce data and to extract a small number of factors depending on the correlation matrix, whereas cluster analysis is performed to further classify elements of different sources on the basis of their similarities.

***Measurements***

Accurate measurement of anthropometry is extremely important for the assessment of physical growth and development. For the 2002 CNNHS survey, a scale and measuring tape for weight and height, respectively, produced by the same factory were provided to each study site. The equipment was recalibrated daily. The investigators were trained for 1 week and only those who passed the exam were qualified for the investigation. The measurements were taken twice by trained investigators following the standard procedure (7), and the average of the 2 measurements was computed. The quality control results indicated that the duplicate measurements in subgroups showed high reproducibility (correlation coefficients of duplicate measurements were 0.99 for height, 0.98 for weight, and 0.97 for waist circumference: WC). We conclude that the quality of the anthropometric measurements in the present study is good (8).

Fasting blood glucose levels were measured by trained technicians, and an oral glucose tolerance test (OGTT) was applied to participants whose fasting glucose was ≥5.5 mmol/l. All of the participants' fasting glucose samples were measured within 4 hours. Every tenth sample was measured twice (correlation coefficients of duplicate measurements was 0.98); at the same time, 1 reference sample, 1 quality control sample, and 1 blind sample were measured before every thirtieth sample(3). Quality control of the serum lipid measurements was carried out in collaboration with the U.S. Center for Disease Control (CDC). Blind serum samples from the U.S.CDC were analyzed in our lab (China CDC) 7 times at regular intervals over the course of the analysis of the samples from the 2002 CNNHS. The relative difference ranged from -7.02% to 1.60% for triglycerides, and from -1.05% to 4.21% for HDL-C. The results showed that blood sample measurements were qualified (3).

***Confounders***

A measure of an association between exposure and outcome is confounded when an explanatory/third factor is associated with both exposure and outcome at the same time (9). In **Chapter 2**, the prevalence of type 2 diabetes (either newly diagnosed using fasting and post-load glucose levels or treated), IGT, and IFG increased with age, and was higher in urban than in rural areas. Smoking is associated with a significantly increased risk of type 2 diabetes (10-12), and poor socioeconomic status may influence the incidence independently, as well as eating behavior and level of physical activity. Therefore, an adjustment was made for living area, education years, smoking, and age in the study of the association between type 2 diabetes and obesity.

Dietary patterns were associated with differences in socioeconomic status **(Chapters 3 and 4)**.Obesity may be an intermediate step in the pathway between diet and type 2 diabetes. The fact that estimates were based on self-report of habitual food intake may have caused bias due to conscious or sub-conscious under- or over-reporting of specific food items (13). Under-reporting of energy intake has been shown to be more prevalent and severe among individuals with a higher BMI (14, 15).When studying the association between dietary intake and diabetes, we therefore adjusted for age, sex, current smoking, physical activity level, family history of diabetes, education level, family income, and BMI or WHtR.

Adjustment for these factors did not change the significant association between dietary factors and type 2 diabetes.

## Issues and challenges

### *Abdominal obesity and type 2 diabetes*

There is substantial literature referring to obesity as a major risk factor in the development of type 2 diabetes. Some studies have used BMI as the measure of obesity (16, 17). It is, however, increasingly recognized that, for a given BMI, central rather than lower body fat distribution confers greater risk of metabolic and cardiovascular complications of obesity (18). Meta-analysis of 119 papers showed that raised abdominal obesity increases the risk of type 2 diabetes more than two fold (19). WHtR includes height as a constant measure and may correct for individual WC. As adults' height does not change much over time, WHtR should be a fairly constant denominator. Therefore, variation in this measure is based mostly on WC. In our study, BMI, WHtR, and WC were all significantly associated with the diagnosis of glucose tolerance abnormalities. The area under the curve (AUC) for BMI was lower than that for WC or WHtR. A cut-off value of WHtR≥0.5 for both men and women can be considered an optimum value for a reduced risk of glucose tolerance abnormalities. This result has been confirmed not only in additional Chinese population studies (20-23), but also in other populations (24-29). In a study among a population of Mexican origin, WHtR was the preferred marker for identifying persons with type 2 diabetes in women; in men, waist circumference was better (2).

### *Dietary patterns and type 2 diabetes*

Dietary patterns reflect a person's food consumption and its change over that person's life span (30, 31). So, they provide comprehensive information about dietary habits and provide a basis on which to make more effective recommendations to manage different diet-related chronic diseases.

The four Chinese dietary patterns identified in a previous study on dietary habits and obesity among Chinese adults were considered to be highly realistic within the nutrition transition framework in China (32). In this thesis, we used these 4 dietary patterns to investigate the association with the presence of newly diagnosed glucose tolerance abnormalities in China (**Chapter 3**), their joint effects with physical activity on the likelihood of metabolic syndrome, and as a stratification factor in **Chapter 5**.

The 'Green Water' pattern was found to have the lowest prevalence of glucose tolerance abnormality (3.9%), whereas thehighest prevalence was found in the'New Affluence' pattern (8.0%).

Food items of similar dietary patterns are different, based on geographic and ethnic characteristics. Numerous dietary patterns, such as 'Mediterranean', 'Dietary Approaches to Stop Hypertension (DASH)', 'Prudent', 'Western', 'Traditional' and 'Healthy' have been studied regarding their relationship with type 2 diabetes (33-37). The inverse association between the 'Mediterranean' dietary pattern and the prevalence of type 2 diabetes was observed in various multi-ethnic studies (33). Several epidemiological studies explained lower odds of having type 2 diabetes(38) and an inverse relation between glucose level (39-41), insulin (33, 38-44), following adherence to the 'Mediterranean' dietary pattern. A 'Prudent' pattern is another dietary pattern characterized by higher consumption of whole grains, vegetables, fruits, poultry/sea foods, legumes, and coffee (34, 45, 46). In an American prospective cohort study, higher adherence to the 'Prudent' pattern was associated with a 16% reduced risk of type 2 diabetes after 12 years of follow-up. However, a 'Western' dietary pattern was associated with an increased risk of almost 60% (34). The 'Western' dietary pattern contains red and processed meat, butter, French fries, refined grains, deserts, potatoes, sweets, and high-fat dairy (34, 45, 46).Comparison of the effects of different diets revealed that dietary patterns containing fiber-rich foods have a protective role in preventing and managing diabetes.

It is concluded that dietary patterns consisting of foods such as vegetables, fruits, whole grains, seeds, and nuts, plus white meat sources like poultry and fish, are associated with a reduced risk of diabetes (47-52). However, dietary patterns rich in processed meat and red meat and refined cereals are associated with higher risks.

Carbohydrates, fat, and protein are the three main sources of energy. Much controversy exists about the relation between the amount and type of dietary fat and carbohydrate and the risk of diabetes (53). Prevailing dietary recommendations promote low-fat, high-carbohydrate diets for the prevention of diabetes, heart disease, and other chronic diseases (54). We used a high fat/protein–low CHO score to evaluate dietary pattern in **Chapter 4**. It has been reported that replacing fat with carbohydrate significantly elevates not only the postprandial glucose level but also postprandial and fasting insulin levels in patients with type 2 diabetes when the total energy intake is constant (55). Hu et al. suggested that dietary recommendations to prevent and manage type 2 diabetes should focus more on the quality of fat and carbohydrate in the diet than quantity alone, in addition to total energy balance (56).

The traditional Chinese diet is different from the Western diet. It includes about 60% energy from carbohydrates, which is nowadays higher than in Western countries(57). The majority of fats in Chinese diets are monounsaturated fatty acids and polyunsaturated fatty acids. Such a low fat–high carbohydrate diet could potentially protect people against type 2 diabetes. It has been reported that a higher percentage of energy intake from cereals is associated with a lower prevalence of diabetes, whereas a higher percentage of energy intake from fat is related with a higher prevalence of diabetes in Chinese populations (58).

In **Chapter 4** and **Chapter 5**, we concluded that the optimal dietary pattern with higher consumption of vegetables and rice and moderate meat consumption, rich in carbohydrate and low in fat, is associated with a decrease in the risk of diabetes. Thus, with the rapid transition from carbohydrates to fat intake in China (59), the prevalence of type 2 diabetes is expected to increase.

***Fetal growth and type 2 diabetes***

Several studies have demonstrated that individuals with a low birth weight have a higher prevalence of obesity, insulin resistance, and type 2 diabetes in adult life than those with a normal birth weight(60). These data have led to the so-called thrifty phenotype hypothesis, i.e. that insulin resistance and type 2 diabetes are the consequences of fetal malnutrition **(Figure 7.1)** (60, 61). Our study found that exposure to severe famine in fetal life increased the risk of hyperglycemia in adulthood (**Chapter 6**). This is consistent with the Dutch Famine Study, which reported higher 2-h glucose and insulin levels among people exposed to famine during fetal life (62-64). This shows that poor maternal nutrition during pregnancy can result in permanent changes to fetal metabolic control systems (62).

In the past 30 years, the nutrition status of the Chinese population has improved significantly. However, malnutrition is still common in China's poor rural areas. In 2002, 30% of children under 5 years had growth retardation, and 14% had a low body weight. The prevalence of growth retardation was highest among the 1-year-old age group, 34.6%, demonstrating that this problem is associated with the improper use of complementary infant foods. The prevalence of anemia among infants and children under the age of 2 was 24.2%, and among the child-bearing women,20.6%(3). Although not exposed to severe famine in utero, people living in poor rural areas in China may be at risk of type 2 diabetes and other nutrition-related disease, especially if they become overweight later in life.

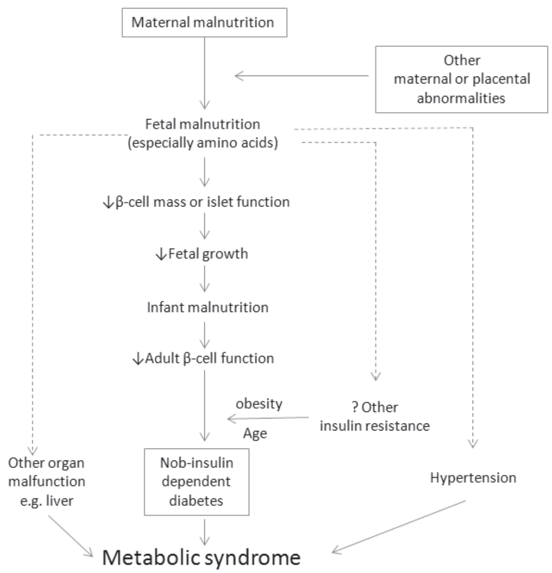


**Figure 7.l Conceptual framework of the thrifty phenotype hypothesis(61)**

## Future research

This thesis is one of the first on diet and type 2 diabetes in China. Our cross-sectional results on dietary patterns and the fat-to-carbohydrate ratio may be confirmed in cohort studies. Some specific foods, such as dairy products (65), fish (47), sugar-sweetened beverages (66), and tea (67) have been reported to be associated with risk of type 2 diabetes in other countries. Additional studies on the association between specific foods and the risk of type 2 diabetes in the Chinese population are needed to examine whether preventive efforts and dietary recommendations should include these foods as well.

The Shanghai Women's Health Study – a population-based prospective cohort study– showed that high intake of foods with a high glycemic index and glycemic load, especially rice, the main carbohydrate-contributing food in this population, may increase the risk of type 2 diabetes in Chinese women (68). A limitation of that study is that the participants were selected from one city. The results should be verified using a nationally representative population in the future.

## Public health implications

Primary prevention of type 2 diabetes was first proposedin 1921 by Elliot Joslin, who wrote: 'There are entirelytoo many diabetic patients in the country…. Therefore,it is proper at the present time to devote attention not alone to treatment, but still more, as in the campaign against the typhoid fever, to prevention. The results maynot be quite so striking or as immediate, but they are sure to come and to be important' (69).

In China, the prevalence of diabetes, which was less than 1% in 1980, has increased significantly in recent decades (70-74). In subsequent national surveys conducted in 1994 and 2000–2001, the prevalence of diabetes was 2.5% and 5.5%, respectively (72, 73). The most recent national survey in 2010 reported that the prevalence of diabetes was 11.6%, and the prevalence of IGT and IFG was50.1%. This represents up to 113.9 million Chinese adults with diabetes and 493.4 million with IGT and IFG (74). Thus, with rapid economic growth and associated industrialization, urbanization, and lifestyle changes, diabetes has reached epidemic proportions in the Chinese population. The health care costs for diabetes are likely become a huge financial burden to patients, their families, and society as a whole (75). To avoid this societal burden, primary prevention of diabetes should be a national priority for China.

Our results, together with the results of other studies, indicated that a healthy dietary pattern, increased physical activity, having a normal body weight, and healthy fetal growth are associated with lower risk of type 2 diabetes.

There is good evidence, also from Chinese studies, that diabetes preventionis possible. Results from the China Da Qing Diabetes Prevention Study showed that, after 6 years, diabetes incidencewas 31%, 46%, or 42% lower than in the control group for dietary, exercise, and combined interventions, respectively (76). The participants with IGT in lifestyle intervention groups had a 43% lower diabetes incidence for up to 14 years after the active intervention ceased, and diabetes onset was delayed an average of 3.6 years (77).

In 2010, the *Chinese Guideline for Preventing and Managing Type 2 Diabetes* recommend that dietary energy intake from total fat should not exceed 30%; energy intake from saturated fatty acids should not exceed 10%, 10%–20% for monounsaturated fatty acids, and less than 10% for polyunsaturated fatty acids; carbohydrate should contribute 50%–60% of total energy; overweight/obesity people should control BMI close to 24 kg/m$^2$; and physical exercise should be 250 to300 minutes every week (78).

The *National Campaign on Healthy Lifestyle for All* has been in operation to prevent and control chronic disease since 2007 in China. The first stage(2007–2015) activity is Health 1-2-1: 1, walk 10,000 steps per day; 2, have a balanced diet and physical activity; 1, be healthy for a lifetime (79). Our study shows that not only people in high socio-economic classes, but also people living in poor areas should pay attention to preventing type 2 diabetes. We suggest that preventive interventions for diabetes should be used at all levels of economic development in China.

We conclude that keeping body weight in the normal range, improving diet quality, and promoting physical activity are the main approaches to prevent type 2 diabetes; this is urgently needed in China.

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# SUMMARY

With the development of the economy and society, and the improvement in living standards, people's lifestyles are changing a lot in China. High energy density diets and low physical activity are becoming increasingly prevalent. The average daily consumption of meats and edible oil increased by 98g and 20g, respectively, in the past 20 years. However, the average consumption of cereals and vegetables per day decreased by 20% in the same period. Meanwhile, the number of TVs and cars is rising rapidly, and public transport is also growing more popular. This social change has not only raised the prevalence of chronic non-communicable diseases, but also strengthened the intensity of their risk factors. Studies have shown that the prevalence of diabetes in China has increased gradually in recent years. However, currently there is little research using nationally representative data to analyze the contributory nutritional factors – especially dietary patterns, physical activity, and obesity.

Therefore, this thesis investigates the association between abdominal obesity, dietary factors, physical activity, and fetal nutrition and type 2 diabetes in China, based on the data analyses of the 2002 China National Nutrition and Health Survey (CNNHS), which is a nationally representative survey, conducted to describe nutrition status, the prevalence of selected diseases, and associated risk factors.

This thesis addresses the following topics: 1) the association between abdominal obesity and type 2 diabetes in Chinese adults; 2) the association of different dietary patterns with the presence of diabetes; 3) the relationship between high fat/protein–low carbohydrate diets and diabetes; 4) the relevance of lifestyle for the presence of metabolic syndrome; and 5) the impact of nutritional status during fetal life on the risk of diabetes in adulthood.

We first studied the association between abdominal obesity and type 2 diabetes in Chinese adults **(chapter 2)**. Using data for adults aged 18–79 years in the 2002 China National Nutrition and Health Survey, we analyzed the prevalence of type 2 diabetes in different levels of three obesity indicators (i.e. body mass index (BMI), waist circumference (WC), and waist/height ratio (WHtR)). The results suggested that high BMI, WC, and WHtR were all associated with the prevalence of type 2 diabetes in both men and women. Among the Chinese population, WHtR was a better indicator than BMI or WC. Compared to non-obese people, overweight and obese people had double the risk of developing diabetes. ROC curve analyses indicated 0.5 as the optimal value for WHtR in both men and women. The risk ratio for diabetes in women with WHtR ≥0.5 was 3.1 times higher than those with WHtR<0.5, and the corresponding figure for men was 2.85. This study used nationally representative data and drew the conclusion that WHtR=0.5 can be considered as an optimum value for preventing diabetes. In **chapter 3** and **chapter 4**, we emphasized the study of the association between dietary patterns in China and the prevalence of diabetes. In **chapter 3**, we used data for 20,210 persons aged 45–69 years who had completed a food frequency questionnaire. Factor analysis was used to divide 28 foods into four dietary patterns, i.e. 'western foods,' 'cereals,' 'expensive foods,' and 'alcohol drinking.' Subsequently, cluster analysis was used to identify four sub-populations with different dietary patterns. Depending on the food consumption in the different clusters, these dietary patterns were named 'Green Water,' 'Yellow Earth,' 'New Affluence,' and 'Western Adopter.' The results showed that persons in the 'Green Water' cluster had the lowest prevalence of diabetes (2.0%). This dietary pattern represented the traditional Chinese diet, with a high consumption of rice and vegetables and a moderate intake of animal foods. The 'Green Water' pattern, composed primarily of plant food, had the lowest prevalence of overweight and obesity.

The 'Yellow Earth' cluster was characterized by lower consumption of meat and dairy, and comprised lower income-earning and less highly educated persons than the other three patterns, but had more overweight, obese, and diabetic individuals. The risk of diabetes in individuals with the 'Yellow Earth' pattern was 1.22 times (95% CI: 1.04–1.43) higher than those with the 'Green Water' pattern. The members of the 'Yellow Earth' cluster were primarily concentrated in the northwest rural areas in China. Malnutrition and over-nutrition coexist in this area. This is a vulnerable group that deserves special attention from researchers and policymakers to help them adopt appropriate measures to improve their health status. People adopting the 'New Affluence' and 'Western Adopter' patterns have broken away from the traditional Chinese food culture. The risk ratio for diabetes in individuals with a 'New Affluence' pattern was 2.05 times (95% CI: 1.76–2.37) higher than those with a 'Green Water' pattern. Adopters of the 'New Affluence' pattern were to a large extent less poor, more highly educated, and in general, lived in urban areas. These Chinese individuals have benefited most socio-economically from the remarkably fast economic growth. The overweight and obesity rates in the 'New Affluence' cluster, as high as 39%, were close to the level of many Western countries. With the rapid development of the Chinese economy, more and more people will gravitate towards the 'New Affluence' cluster.

The traditional Chinese dietary pattern was based on cereals, but the diet in China has changed dramatically in the last two decades. The consumption of total fat has increased significantly. The energy intake from fat increased from 18% in 1982 to 30% in 2002. However, the proportion of total dietary energy intake from carbohydrate decreased from 71% in 1982 to 59% in 2002. In **chapter 4**, we used the high fat/protein–low carbohydrate diet score to investigate the association between different high fat/protein–low carbohydrate diet scores and diabetes. The results showed that the risk ratio for diabetes in individuals with high scores was 2.75 times higher than those with low scores (95% CI: 2.09–3.61). Therefore, the dietary pattern of Chinese populations is undergoing a rapid transition from high carbohydrate with low fat (resembling the 'Green Water' pattern) to high fat with low carbohydrate (resembling the 'New Affluence' pattern). It can markedly increase the risk of a range of chronic diseases such as obesity and diabetes.

Physical activity and diet are key points to prevent and control diabetes. In **chapter 5**, we analyzed the difference in the risk of developing metabolic syndrome among individuals with different physical activity levels and dietary patterns. The results demonstrated significant physical activity and dietary patterns interaction in relation to metabolic syndrome (MS). Participants with a combination of sedentary activity and a 'Yellow Earth' dietary pattern or a 'Western/ New Affluence' dietary pattern both had more than three times (95% CI: 2.8–6.1) higher odds of MS than active people with a 'Green Water' dietary pattern. The associations between dietary patterns and MS attenuated after adjusting for BMI, indicating that the associations between dietary patterns and MS risk may be partially mediated through dietary effects on overall obesity. Thus, encouraging healthy dietary patterns and moderate physical activity should help towards preventing MS.

In **chapter 6**, we analyzed and compared the prevalence of hyperglycemia and diabetes among individuals born before, during, and after the Chinese famine (1959–1961). The results showed that fetal exposure to the severe Chinese famine increased the risk of hyperglycemia in adulthood. If the dietary pattern was not balanced in adulthood, it might further increase susceptibility to hyperglycemia in those who experienced fetal exposure to famine.

In summary, the prevalence of diabetes in China is rather low compared to developed countries. However, overweight and obesity are important factors that can increase its prevalence. With the overweight and obesity rates of Chinese populations rapidly rising, the prevalence of diabetes is on an upward trend. We found significant physical activity–dietary patterns interaction in relation to MS. Individuals with a healthy diet and an active lifestyle are less likely to succumb to MS.

In **chapter 7**, the main findings of this thesis are summarized and their interpretation, methodological issues and public health relevance are discussed. In addition, recommendations for future research are addressed. Overall, the findings presented in this thesis support the current recommendation of keeping body weight in the normal range, improving diet quality, and promoting physical activity as the main strategies to prevent diabetes.

Therefore, we should intensify public nutrition education, advocate the preservation of traditional Chinese eating behaviors, reduce consumption of fat, encourage moderate physical active, and lead people to make healthier lifestyle choices.

# Samenvatting

Door de snelle economische en sociale ontwikkelingen in China verbetert de levensstandaard van veel Chinezen en verandert hun levensstijl. Deze veranderingen zijn niet altijd gunstig. Een dagelijkse voeding met een hoge energiedichtheid in combinatie met weinig bewegen komen steeds vaker voor. In de afgelopen 20 jaar steeg de gemiddelde dagelijkse consumptie van vlees en eetbare olie met 98g en 20g, respectievelijk. Tegelijkertijd daalde het dagelijks gebruik van granen en groenten met 20%. Ook is het aantal televisies en het aantal auto's ondertussen snel gestegen en wordt ook het openbaar vervoer steeds populairder. Niet alleen is er een toename te zien in de prevalenties van verschillende chronische niet-overdraagbare aandoeningen, zoals diabetes, maar zijn ook de prevalenties van de bijbehorende risicofactoren flink toegenomen. De afgelopen jaren hebben verschillende studies aangetoond dat de prevalentie van diabetes in China geleidelijk aan is gestegen. Op dit moment echter is er in China op nationaal niveau nog nauwelijks onderzoek gedaan naar de rol van voedingsfactoren, in het bijzonder voedingspatronen, en de rol van lichamelijke beweging en overgewicht bij het optreden van diabetes.

In dit proefschrift beschrijven we het onderzoek naar het verband tussen overgewicht/ abdominale obesitas, voedingsfactoren, lichamelijke activiteit, en voeding van het ongeboren kind (foetale voeding) en type 2 diabetes in China, gebaseerd op data-analyses van de in 2002 uitgevoerde "China National Nutrition and Health Survey" (CNNHS ); dit is een landelijk representatief onderzoek, uitgevoerd om de voedingsstatus, de prevalentie van geselecteerde ziekten zoals diabetes en hart- en vaatziekten en de daarbij behorende risicofactoren te beschrijven. In dit proefschrift komen de volgende onderwerpen aan bod: 1) de associatie tussen abdominale obesitas en type 2 diabetes in de Chinese volwassenen; 2) het verband tussen verschillende voedingspatronen en de aanwezigheid van diabetes ; 3) het verband tussen vetrijke/ koolhydraatarme voeding en diabetes; 4) de relatie tussen levensstijl en de aanwezigheid van metabool syndroom (combinatie van risicofactoren die kunnen leiden tot o.a. diabetes); en 5) het effect van de voedingstoestand tijdens het ongeboren leven op het risico van diabetes op volwassen leeftijd.

We bestudeerden eerst de relatie tussen abdominale obesitas en het krijgen van type 2 diabetes bij Chinese volwassenen (**hoofdstuk 2**) . Met behulp van gegevens van volwassenen tussen de 18-79 jaar uit de CNNHS analyseerden we de relatie tussen de prevalentie van type 2 diabetes en drie verschillende indicatoren van overgewicht: d.w.z. body mass index (BMI), buikomvang (WC), en de ratio tussen buikomvang en lengte (WHtR). De resultaten laten zien dat alle drie indicatoren positief waren met de prevalentie van type 2 diabetes bij zowel mannen als vrouwen. Daarbij was de WHtR een betere indicator dan de BMI of

WC in deze populatie. Mensen met overgewicht of obesitas, gebaseerd op BMI, WC of WHtR, hadden in vergelijking met mensen zonder overgewicht een meer dan twee keer zo hoge prevalentie van diabetes. In deze populatie werd de optimale WHtR voor het voorspellendvan de aanwezigheid van diabetes berekend door middel van ROC-curves. Zowel bij mannen als bij vrouwen bleek de optimale waarde voor de WHtR 0.5. Bij vrouwen was risico op diabetes 3.1 keer hoger bij een WHtR ≥0,5 in vergelijking tot met WHtR <0,5. Voor mannen was het risico 2.85 keer hoger.

In de hoofdstukken 3 en 4 beschrijven we de relatie tussen verschillende voedingspatronen en de prevalentie van diabetes. In **hoofdstuk 3** hebben we gebruik gemaakt van gegevens van >20.000 personen tussen de 45-69 jaar, die een voedselfrequentievragenlijst hadden ingevuld. We gebruikten factoranalyse om 28 voedingsmiddelen te verdelen in vier voedingspatronen, dat wil zeggen 'westers voedsel , 'granen', 'duur voedsel', en 'alcohol drinken'. Vervolgens werd cluster-analyse gebruikt om vier subpopulaties (clusters) met verschillende voedingspatronen te identificeren. Afhankelijk van de voedselconsumptie in de verschillende clusters werden deze voedingspatronen genaamd 'Green Water', 'Yellow Earth', 'New Affluence', en 'Western Adopter'. De resultaten toonden aan dat personen in het cluster 'Green Water' de laagste prevalentie van diabetes (2,0%) hadden. Dit voedingspatroon vertegenwoordigde het traditionele Chinese dieet, met een hoge inname van rijst en groenten en een lage inname van dierlijk voedsel. Het 'Green Water' patroon, dat voornamelijk samengesteld is uit plantaardig voedsel, had ook de laagste prevalentie van overgewicht en obesitas ten opzichte van de andere subpopulaties.

Het 'Yellow Earth' patroon werd gekenmerkt door een lagere consumptie van vlees en zuivel. Personen met dit voedingspatroon hadden een lager inkomen en waren minder hoogopgeleid, hadden vaker overgewicht, obesitas en diabetes dan in de andere drie patronen. Het risico van diabetes bij personen met het 'Yellow Earth' patroon was 1,22 maal (95% BI: 1,04-1,43) hoger dan die met het 'Green Water' patroon. De personen met het 'Yellow Earth' patroon kwamen voornamelijk uit de noordwestelijke landelijke gebieden in China. In dit gebied komen zowel ondervoeding als overvoeding voor. Dit is een kwetsbare bevolkingsgroep die bijzondere aandacht verdient van onderzoekers en beleidsmakers om hen te helpen de nodige maatregelen te treffen om hun gezondheidstoestand te verbeteren. Mensen die de voedingspatronen van het 'New Affluence' patroon en het 'Western Adopter' patroon hebben over genomen hebben gebroken met traditionele Chinese eetcultuur. Het risico op diabetes van mensen in het 'New Affluence' patroon was 2,05 maal (95% BI : 1,76-2,37 ) hoger dan die met een 'Green Water' patroon. De personen met het 'New Affluence' patroon waren voor een groot deel minder arm en hoger opgeleid woonden voornamelijk in stedelijke gebieden. Deze groep Chinezen heeft sociaaleconomisch het meest geprofiteerd van de opmerkelijk snelle economische groei. Opmerkelijk is dat het percentage overgewicht en obesitas in het patroon van 'New Affluence' dicht bij het niveau van veel westerse landen komt (39%). Met de snelle ontwikkeling van de Chinese economie zullen meer en meer mensen neigen naar dit patroon.

Het traditionele Chinese voedingspatroon, dat was gebaseerd op granen, wordt steeds meer vervangen door andere voedingspatronen. De consumptie van totaal vet is sterk toegenomen; de energie-inname uit vet is gestegen van 18% in 1982 tot 30% in 2002. Het aandeel van koolhydraten ten opzichte van de totale energie-inname is daarentegen sterk gedaald van 71% in 1982 naar 59% in 2002. In **hoofdstuk 4** gebruikten we een 'rijk-aan-vet/ arm-aan-koolhydraten' dieet score om de associatie tussen deze score en diabetes te onderzoeken. De resultaten toonden aan dat het risico voor diabetes bij personen met een hoge score 2,75 (95%-BI : 2,09-3,61 ) keer hoger was dan voor personen met een lage score. We zien dat het voedingspatroon van de Chinese bevolking een snelle verschuiving maakt van een voeding met een hoog koolhydraat gehalte en een laag vetgehalte (dat lijkt op het 'Green Water' patroon ) naar een voeding met een hoog vet gehalte en een laag koolhydraat gehalte (dat lijkt op het 'New Affluence' patroon). Hiermee neemt het risico op verschillende chronische ziekten, zoals obesitas en diabetes, aanzienlijk toe.

Lichamelijke beweging en gezonde voeding zijn belangrijk om diabetes te voorkomen en te beheersen. In **hoofdstuk 5**, analyseerden we het verschil in het risico op het ontwikkelen van het metabool syndroom bij mensen met verschillende lichamelijke activiteit en eetgewoonten. De resultaten toonden een synergie aan tussen lichamelijke beweging en verschillende voedingspatronen in relatie tot het metabool syndroom. Deelnemers met een combinatie van een zittend bestaan en een 'Yellow Earth' of 'Western Adopter'/ 'New Affluence' voedingspatroon hadden allebei een meer dan drie keer (95%-BI: 2,8-6,1) zo hoge kans op metabool syndroom dan actieve mensen met een 'Green Water' voedingspatroon. Deze associaties tussen voedingspatronen en metabool syndroom waren minder sterk na correctie voor BMI, wat aangeeft dat het verband tussen voedingspatronen en het risico op metabool syndroom gedeeltelijk verklaard kan worden door het effect van voeding op overgewicht en obesitas. Dus het stimuleren van een gezond voedingspatroon en lichamelijke beweging kan bijdragen aan het voorkómen van metabool syndroom.

In **hoofdstuk 6** hebben we de prevalentie van een te hoge bloedsuikerspiegel (hyperglycemie) of diabetes bij mensen geboren vóór, tijdens en na de Chinese hongersnood (1959-1961) vergeleken. De resultaten toonden aan dat blootstelling van ongeboren kinderen aan de strenge Chinese hongersnood een verhoogd risico gaf op een te hoge bloedsuikerspiegel tijdens volwassenheid. Als het voedingspatroon niet evenwichtig was tijdens volwassenheid, was de gevoeligheid voor een te hoge bloedsuikerspiegel verhoogd bij degenen die hongersnood hadden meegemaakt tijdens hun ongeboren leven. De prevalentie van diabetes in China is tot op heden vrij laag in vergelijking met ontwikkelde landen. Echter, overgewicht en obesitas zijn belangrijke risicofactoren die de prevalentie kunnen verhogen en we zien dat deze factoren steeds vaker voorkomen in China. Dit zal mogelijk leiden tot een opwaartse trend in de prevalentie van diabetes. Voeding kan een belangrijke rol spelen bij het voorkomen en beheersen van een te hoge bloedsuikerspiegel en diabetes. In relatie tot het metabool syndroom vonden we dat lichamelijke beweging in combinatie met een gezond voedingspatronen elkaar versterken. Personen met een gezonde voeding en een actieve levensstijl krijgen waarschijnlijk minder vaak metabool syndroom .

In **hoofdstuk 7** worden de belangrijkste bevindingen van dit proefschrift samengevat en worden de interpretatie, methodologische aspecten en de relevantie voor de volksgezondheid besproken. Daarnaast worden aanbevelingen voor toekomstig onderzoek gedaan. Alles bij elkaar genomen ondersteunen de bevindingen gepresenteerd in dit proefschrift de huidige aanbevelingen.

De belangrijkste strategieën om diabetes te voorkomen omvatten onder andere het op peil houden van het lichaamsgewicht, het verbeteren van kwaliteit van de voeding, en het bevorderen van lichamelijke activiteit. Het is daarom belangrijk om het publieke onderwijs met betrekking tot gezonde voeding te stimuleren en te intensiveren. Hierbij moet gepleit worden voor het behoud van de gezonde traditionele Chinese eetpatroon en voor het beperken van vet, het bevorderen van lichamelijke beweging en het stimuleren van mensen om gezondere levensstijl keuzes te maken.

# 总结

社会经济发展和物质生活水平的提高，导致人们生活水平的诸多变化，高能量密度膳食、低体力活动和久坐少动的生活方式越来越普及。二十年间，中国居民平均每天肉类食物和食用油的摄入量分别增加了 98g 和 20g。而粮谷类食物和蔬菜消费量在过去 20 年间降低了 20%。与此同时，电视机和汽车拥有量迅速增加，公共交通工具也越来越普及。这一社会的变迁使得慢性非传染性疾病患病率上升及其危险因素的强度不断增加。研究发现，近年来中国糖尿病的患病率逐渐增加，但目前利用全国代表性数据分析糖尿病的营养因素，特别是膳食因素的研究很少。

本论文利用 2002 年中国居民营养与健康状况调查这个具有全国代表性的调查资料对分析中国成年人糖尿病与中心型肥胖、膳食因素、身体活动以及生命早期营养的相关性。

论文包括以下内容 1）中国成年人中心型肥胖与 II 型糖尿病的关系 2）不同膳食模式与糖尿病发生的相关性 3）高脂肪/蛋白质-低碳水化物膳食模式与糖尿病的关系 4）生活方式与代谢综合症的关系 5）生命早期的营养状况对成年人期糖尿病发生的影响。

我们首先中国成年人中心型肥胖与糖尿病的关系（**第 2 章**），选择了 2002 年中国居民营养与健康调查中 18-79 岁的成年人，分析了三种肥胖评价指标（BMI，腰围，腰围身高比）的不同水平下糖尿病的发生情况，结果显示，无论是男性还是女性，BMI，腰围，腰围身高比都与糖尿病的发生率显著性相关，超重肥胖的人与非超重肥胖的人相比，发生糖尿病的风险增加 1 倍。三个指标相比较，腰围身高比作为中国人糖尿病的发生的预测指标更好。利用 ROC 的方法确定腰围身高比为 0.5 作为切点，女性腰围身高比大于 0.5 的人群发生糖尿病的可能性是小于 0.5 的人群的 3.1 倍，男性是 2.85 倍。本研究采用了具有中国人群代表性的数据，所得结论“腰围身高比为 0.5 作为预防糖尿病切点”具有重要的公共卫生意义。

在**第 3 章**和**第 4 章**中，我们重点研究了中国人群的膳食模式与糖尿病发生率的关系。在论文第三章利用 20,210 名 45-59 岁成年人的 FFQ 膳食调查数据，采用因子分析的方法，对将 28 类食物分成了 4 组，“西式食物”、“谷类”、“高档食物”、“酒精饮料”。在此基础上采用聚类分析的方法将人群分成了 4 个不同饮食特点的亚人群，分别是根据各人群食物消费特点，分别命名为“黄土高坡”、“江南水乡”、“小康之家”、 “西洋情调”。结果显示“江南水乡”人群的糖尿病患病率最低，他们的膳食模式保留着中国传统的饮食习惯，以米饭和蔬菜为主，并有适度的肉类摄入。这种以植物性食物为主的膳食使得这部

分人群的超重和肥胖率最低，这提示我们，中国传统的饮食是比较健康的，应提倡人们保留传统的饮食习惯。“黄土高坡”人群尽管肉类、奶制品的摄入水平都很低，相对来说他们是低收入和低文化水平的人群，但他们的超重和肥胖率、糖尿病率却比较高。黄土高坡人群发生糖尿病的风险是江南水乡人群的1.22 倍。这部分人群主要居住在中国西部农村地区，人群中仍存在着营养不良的问题，也就是说，他们承受着双重负担—营养不良和营养失衡。他们属于“脆弱人群”，国家和政府应特别关注这部分人群，采用相应的措施改变“黄土高坡”人群的健康状况。“小康之家”和“西洋情调”打破了中国传统的饮食模式，由此带来了较高的超重和肥胖的发生，同时糖尿病的发生率高，“小康之家”人群发生糖尿病的风险是江南水乡人群的 2.05 倍。这些人是中国经济发展的最大受益者，他们较为富有、文化水平较高、居住在城市地区。“小康人家”人群高达 39%的超重和肥胖率已经接近很多西方国家的水平。随着中国经济的飞速发展，中国将会有越来越多的人进入“小康人家”这一群体。

在传统的膳食结构中是以谷类为主，近 20 年中国人群的膳食结构发生很大变化，脂肪摄入量明显增加，从脂肪供能比从 1982 年的 18%，增加到 2002 年的 30%，碳水化合物的比例明显下降，从 1982 年的 71%下降到 2002 年的 59%。在第四章中我们采用高脂肪/蛋白质-低碳水化合物评分的方法，研究不同的高脂肪/蛋白质-低碳水化合物的模式是否与糖尿病的发生存在一定的关系。结果显示，高脂肪/蛋白质-低碳水化合物得分高的人群发生糖尿病的风险是低分值人群的 2.75 倍（95%CI：2.09-3.61）。由此可以看出，中国人群膳食结构的变迁，从高碳水化合物，低脂肪的膳食结构（类似于江南水乡模式）走向低碳水化合物、高脂肪的膳食结构（类似于小康之家），使得人群发生肥胖、糖尿病等慢性疾病的风险显著增加。

身体活动与膳食是预防和控制糖尿病及其他营养相关疾病的重要手段，在**第 5 章**中，我们分析比较不同的膳食模式下，具有不同身体活动水平的人发生代谢综合征的风险是否具有差异。结果显示，身体活动水平与膳食模式对代谢综合症发生有交互作用，“黄土高坡”膳食模式和“小康人家”膳食模式加上久坐少动的身体活动水平发生代谢综合征的风险是“江南水乡”膳食模式加上非常活跃的身体活动水平人群的 3 倍以上（95%CI：2.8-6.1），这一结果与其他人群的研究结果一致。膳食模式对代谢综合征的影响在控制了 BMI 之后，就没有显著性了，说明膳食模式对代谢综合征的作用主要是在肥胖方面。 因此鼓励健康膳食模式。

在**第 6 章**中，分析比较了在中国饥荒时期（1959 年-1961 年）出生、在饥

荒前出生以及饥荒后出生的人群的高糖血症和糖尿病的患病率，结果显示，在生命早期处于严重饥荒状态，增加成年后发生高糖血症的风险。如果成年后膳食模式不均衡会进一步增加患病的风险。

综上所述，虽然与发达国家相比，中国糖尿病患病率还比较低，超重和肥胖是糖尿病患病率增加的重要危险因素，中国人群超重肥胖率的快速增加，预示着糖尿病患病率将呈不断上升趋势。本研究发现身体活动与膳食模式对代谢综合征有协同作用，健康的膳食模式和充分的身体活动减少发生代谢综合征的风险。

**第 7 章**中，对本论文的研究方法、主要内容、研究意义进行了总结。同时提出对未来研究工作的建议。本论文得到的主要结论能够支持当前预防糖尿病的所采取的主要措施，即保持体重维持在正常范围、提高膳食质量以及增加身体活动等。

因此，应加强公众营养教育，倡导健康膳食模式，减少脂肪摄入量，鼓励适度体力活动，控制超重肥胖的发生，引导民众选择健康生活方式。

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特别感谢杨晓光教授，作为 2002 年中国营养调查的项目负责人，十几年来在他的指导下，我的工作能力有了很大的提升，也为我能顺利完成博士论文研究奠定了坚实的基础。

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# ABOUT THE AUTHOR

**Curriculum Vitae**

**List of publications**

**Educational training**

## Curriculum Vitae

Yuna He was born on Feb 20th 1967, in Beijing, China. After she finished her secondary school education in 1985, she started the bachelor program “Applied Mathematic” in Beijing Union University.

From August 1989 by now, Yuna He has been working in National Institute for Nutrition and Food Safety, Chinese Center for Disease Control and Prevention. During this period, she attended a Master degree program (2002-2004) in Peking Union Medical College with a specialization in Social Medicine and Health Management. She enrolled in several scientific projects in the field of dietary measurements and nutrition assessment, including ‘National nutrition and health survey in 2002’, ‘National nutrition and health surveillance in 2010-2014’, ’Establishing the Rapid Dietary Quality Assessment System Based on The Dietary Guidelines for Chinese Residents and Chinese Food Guide Pagoda’, ‘Dietary supplement use in Beijing’ and ‘China-US collaboration Project on Chinese children and families cohort study’.

From Oct.2006, she started her Sandwich PhD program between INFS and Wageningen University, and will defence her thesis on 2 June 2014 in Aula of Wageningen.

## List of Publications

Publication in Peer-Reviewed English Journnals

1. Dong Wang*, Yuna He*, Yanping Li, Dechun Luan, Xiaoguang Yang, FengyingZhai, Guansheng Ma. Joint Association of Dietary Pattern and Physical Activity Level with Cardiovascular Disease Risk Factors among Chinese Men: A Cross-Sectional Study. PLOS ONE. June 19,2013 (*Equal contribution)
2. YunaHe, YanpingLi, JianqiangLai, Dong Wang,, JianZhang, Ping Fu, XiaoguangYang, Lu Qi. Dietary patterns as compared with physical activity in relation to metabolic syndrome among Chinese adults. Nutrition, Metabolism & Cardiovascular Diseases (2013),23(10) : 920–928
3. YunaHe, Edith J.M. Feskens, YanpingLi, Jian Zhang, Ping Fu, GuanshengMa and XiaoguangYang. Association between high-fat-low-carbohydrate-diet score and new diagnosed type 2 diabetes among Chinese population, 2012, Biomedical and Environmental Sciences ,25(4):373-382.
4. Yanping Li*, Yuna He*, JianqiangLai,Dong Wang, Jian Zhang, Ping Fu, Xiaoguang Yang , and Lu Qi. Dietary Patterns are Associated with Stroke in Chinese Adults.2011 J.Nutr. 141:1834-1839(*Equal contribution)
5. Yanping Li*,Yuna He* ,Lu Qi , Vincent W.Jaddoe, Edith J.M. Feskens, Xiaoguang Yang, Guansheng Ma, and Frank B. Hu. Exposure to the Chinese famine in early life and the risk of hyperglycemia and type 2 diabetes in adulthood. Diabetes, 2010 ,59:2400-2406
6. YunaHe,FengyingZhai,Guansheng Ma, Edith J.M Feskens, Jian Zhang, Ping Fu, Pieter Van't Veer and Xiaoguang Yang. Abdominal obesity and the prevlence of diabetes and the prevalence of diabetes and intermediate hyperglycaemia in Chinese adults. Public Health Nutrition 2009 Aug.,12(8) 1078-1084
7. Yuna He, Guansheng Ma ,FengyingZhai, Yanping Li, Yisong Hu, Edith J.M Feskens, Xiaoguang Yang.. Dietary patterns and the prevalence of glucose tolerance abnormalities in Chinese adults. Diabetes Care.2009 Nov，32（11）：1972-1976
8. Xiaoyong Zhang, Hans Dagevos, YunaHe,Ivo Van Der Lans, FengyingZhai. Consumption and corpulence in China-A consumer segmentation study based

on the food perspective. Food Policy 33(2008)37-47(Correspondence Author)

9. Yanping Li, Vincent W.Jaddoe,Lu Qi, Yuna He, Dong Wang, Jianqiang Lai, Jian Zhang, Ping Fu, Xiaoguang Yang, Frank B.Hu. Exposure to the Chinese Famine in Early life and the Risk of Metabolic Syndrome in Adulthood. Diabetes Care, 2011 April 34:1014-1018
10. Yanping Li, Vincent W.Jaddoe,Lu Qi, Yuna He, Jianqiang Lai, Jiansheng Wang, Jian Zhang, Yisong Hu, Eric L.Ding, Xiaoguang Yang, Frank B. Hu and Guansheng Ma. Exposure to the Chinese Famine in Early life and the Risk of Hypertension in Adulthood. Journal of hypertension, 2011 29:1085-1092
11. Yanping Li, Nicole M Wedick, Jianqiang Lai, Yuna He, Xiaoqi Hu, Ailing Liu, Songming Du, Jian Zhang, Xiaoguang Yang , Chunming Chen, Frank B. Hu and Guansheng Ma . Lack of dietary diversity and dyslipidaemia among stunted overweight children: the 2002 China National Nutrition and Health Survey. 2011 . Public Health Nutrition 14(5), 896-903
12. Dong Wang, Yuna He, Yanping Li, Dechun Luan, Xiaoguang Yang, FengyingZhai, Guansheng Ma. Dietary patterns and hypertension among Chinese adults: a nationally representative cross-sectional study. 2011 ,BMC Public Health.11:925
13. Shuqian Liu, Wenyu Wang, Jian Zhang, Yuna He, Chonghua Yao, ZhechunZeng, JianhuaPiao, Barbara V. Howard, Richard R.Fabsits, Lyle Best, Xiaoguang Yang, Elisa T. Lee. Prevalence of Diabetes and Imparied Fasting Glucose in Chinese adults, China National Nutrition and Health Survey, 2002. 2011, Preventing Chronic Disease 8(1):
14. Hans Dagevos, Yuna He, Xiaoyong Zhang, Ivo van der Lans andFengyingZhai. Relationships among healthy lifestyle beliefs and body mass index in urban China. International Journal of Consumer Studies.2010

Publication in Chinese Journal

1. Yuna He, Fengying Zhai, Xiaoguang Yang, Keyou Ge. The Chinese Diet Balance Index Revised. ACTA Nutrimenta SINICA, 2009 Dec. Vol. 31 No 6
2. Yuna He,Zhen Yang, Jun Xu et.al. Vitamins and minerals intake from diet and dietary supplement in Beijing Adult. ACTA Nutrimenta SINICA, 2008, Vol.30 No 2, 125-129

3. Yuna He,Zhen Yang, Jun Xu et.al. Dietary supplement use in Beijing. Journal of Hygiene Research 2008,37(1)
4. Yuna He, Fengying Zhai, Zhihong Wang,et..al. Status of dietary calcium intake of Chinese residents. Journal of Hygiene Research 2007,36(5)
5. Yuna He, Fengying Zhai, Yisong Hu, et al . Study on food and antioxidant intake in smokers and non-smokers in China. Chinese Journal of Epidemiology. 2006,27(9).

Book chapters in Chinese

1. Report of 2002 China National Nutrition and Health Survey (1): Summary Report. Beijing: People's Medical Publishing House. 2006.
2. Report of 2002 China National Nutrition and Health Survey (2): Dietary and Nutrition Report. Beijing: People's Medical Publishing House. 2006.
3. Report of 2002 China National Nutrition and Health Survey (10): Dietary and Nutrition Dataset. Beijing: People's Medical Publishing House. 2008

## Overview of completed training activities

### Optional courses and activities

- Preparation research proposal,2006
- HNE course Epidemiology and Public Health,2006
- HNE course Analytical Epidemiology,2008
- Staff Seminars in WUR, 2006,2007,2008
- Staff Seminars in China CDC, 2006-2013
- Journal Club , Division of Human Nutrition, 2006

### General courses

- PhD study tour USA, 2007
- Workshops on revising Chinese dietary guideline ,2007 (total 30 days)
- Workshops on revising Chinese DRIs, 2012-2014 (total 20 days)
- Workshop on ‘A comprehensive global monitoring framework and voluntary global targets for the prevention and control of NCDs’,2013-2014

### Discipline specific activities

- VLAG course nutritional and lifestyle epidemiology 2006
- Presented at VLAG symposium “from soil to healthy people”, Netherlands , 2006
- Presented Farewell symposium Martijn Katan: Nutrition Top Three, Wageningen, Netherlands, 2006
- Oral presentation ' Consumption and Obesity in China'. 17th Annual IAMA Forum & Symposium in Parma, Italy, 2007
- Oral presentation ' Consumption and Corpulence in China'. LEI, Netherlands,2007
- Oral presentation ' Abdominal obesity and (pre-)diabetes in China'. 17th European Congress on obesity, Amsterdam, Netherland, 2009
- Poster presentation ' Dietary pattern and metabolic syndrome in China'. International congress of Nutrition 2009 , Thailand

- Oral presentation ' Recommendation value for Chinese Dietary Guideline'. Symposium on Chinese dietary guideline. Xi An, China, 2007
- Oral presentation: The Dietary and Health Status of Chinese population. Conference on Oral Health Through Fluoride for China and Southeast Asia, Beijing, China, 2007
- Oral presentation 'Food consumption and Obesity'. Symposium on Chinese nutrition status , nutrition improvement and diet related chronic diseases. Beijing ,China, 2008
- The 10th National Nutrition Conference of China Nutrition Society. Beijing , China ,2008
- Oral presentation ' Chinese food and nutrition intake in 2010', The 11th National Nutrition Conference of China Nutrition Society, Hangzhou , China ,2013
- Presented at Workshop on Policy and Strategy for Malnutrition Improvement , Beijing , China. 2008
- Oral presentation ' Dietary survey in China'. Workshop on Nutrition and Health Organized by China CDC and RIVM, Beijing , China 2013
- Presented at Conference on lifestyle and chronic disease prevention in China, Beijing,2007
- Oral presentation ' Data management, report and policy development'. Workshop on Nutrition Surveillance , Beijing ,China, 2011
- Oral presentation ' Dietary Pattern and Chronic Disease' Workshop on Nutrition studies in China, Beijing ,China, 2011