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Association between risk of type 2 diabetes and changes in energy intake at breakfast and dinner over 14 years: a latent class trajectory analysis from the China health and nutrition Survey, 1997–2011

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ABSTRACT

Objective This study aimed to investigate the association between the trajectories of energy consumption at dinner versus breakfast and the risk of type 2 diabetes (T2D).

Design Cohort study.

Setting The study was conducted in China.

Participants A total of 10 727 adults, including 5239 men and 5488 women, with a mean age of 42.7±11.2 years and a mean follow-up time of 9.1 years, met the study criteria and completed a questionnaire about energy intake and diabetes status from the China Health and Nutrition Survey in 1997–2011.

Primary outcome measures Participants were divided into subgroups based on the trajectories of the ratio of energy consumption at dinner versus breakfast. Cox multivariate regression models were used to explore the associations between different trajectories and the risk of T2D after adjustment for confounders and their risk factors. Mediation analysis was performed to explore the intermediary effect of triacylglycerol (TG), total cholesterol (TC), uric acid (UA) and apolipoprotein B (ApoB) between the trajectories and the risk of T2D.

Results For energy consumption at dinner versus breakfast, compared with a low-stable trajectory, the adjusted HR of T2D in low-increasing from early-stage trajectory was 1.29 (95% CI 1.04 to 1.60). TG, TC, UA and ApoB were significantly higher in low-increasing from early-stage trajectory than other trajectories and play partial regulation roles between trajectories and T2D.

Conclusions This study emphasised the harmful effect of a gradual increase in the ratio of energy consumption at dinner versus breakfast from early stage on the development of T2D and partially mediated by TG, TC, UA and ApoB, highlighting that it is necessary to intake more energy at breakfast compared with dinner to prevent T2D in adults.

Strengths and limitations of this study

- The data come from the CNHS, which is a database with high quality and integrity and represents 47% of the Chinese population based on the 2010 census.
- This study was the first to explore the relationship between breakfast and dinner energy intake and the incidence of type 2 diabetes (T2D) using latent class trajectory analysis.
- This study showed the advantage of using a latent class trajectory model compared with a logistic method to study the relationship between the ratio dinner energy intake divided by breakfast energy intake and the risk of T2D.
- Self-reporting of T2D led to a reduction in the incidence of T2D in this study.
- This study included only Asian participants, which was likely to limit the generalisability of our findings to other ethnic populations.

INTRODUCTION

Type 2 diabetes (T2D), which comprises more than 95% of diabetes in the world, is considered one of the important public health challenges in modern society especially in China and will increase to 439 million patients by the year 2030.[1–3] The distribution of energy consumption at dinner and breakfast, which is an adjustable factor, plays important roles in the occurrence and development of T2D.[4–7] In recent years, some studies have demonstrated that the circadian clock system can interact with nutrients to influence bodily functions, putting forward a new area in the field of nutrition which is described as 'chrononutrition.'[8 9] Meal timings or chrononutrition is an important factor influencing circadian rhythm and can contribute to circadian misalignment causing T2D.[10] High energy at breakfast or time-restricted feeding during the evening can promote clock gene expression, and high energy at dinner or skipping breakfast

Table 1 Baseline characteristics by different trajectories of Z energy consumption at dinner versus breakfast

Variables	T1 (n=6883)	T2 (n=1425)	T3 (n=1565)	T4 (n=854)	P value
Case (%)	511 (7.4)	119 (8.4)	130 (8.3)	81 (9.5)	<0.001
Age (years)	43.2 (15.9)	46.2 (17.1)	42.5 (12.5)	33.2 (11.7)	<0.001
Current smoking (n (%))	2031 (29.5)	439 (30.8)	508 (32.5)	235 (27.5)	0.038
Drinking (drinks/week)	4.1 (11.5)	3.8 (10.5)	4.6 (12.0)	4.4 (13.2)	0.191
PAL (MET-hour/week)	76.2 (108.1)	54.7 (93.1)	83.8 (107.9)	102.8 (109.6)	<0.001
High school education ((n (%))	1609 (22.4)	222 (15.6)	384 (24.5)	254 (29.7)	<0.001
Total energy (kcal/day)	2256.5 (632.9)	2365.5 (661.5)	2252.1 (584)	2195.7 (565.4)	0.228
Total protein (g/day)	68.6 (23.5)	70.3 (23.3)	69.6 (21.9)	68.8 (22.1)	0.168
Total fat (g/day)	66.6 (35)	72 (38.3)	74.3 (34.3)	72.2 (31.7)	<0.001
Total carbohydrate (g/day)	349.3 (122.2)	361.4 (123.7)	328.4 (112.8)	320.7 (114.3)	<0.001
Energy at breakfast (kcal/day)	637.3 (253.1)	606.2 (244.1)	507.5 (218.8)	467 (230.7)	<0.001
Energy at dinner (kcal/day)	800.8 (263.5)	903.5 (299.5)	899.1 (262.8)	884.4 (244.8)	<0.001
Urban index	57.8 (20.9)	57.0 (18.8)	63.0 (17.7)	62.4 (17.3)	<0.001
BMI (kg/m^2)	22.8 (3.4)	22.1 (3.2)	22.5 (3.2)	22 (3.3)	<0.001
Hypertension (n, (%))	1428 (20.7)	269 (18.9)	276 (17.6)	74 (8.7)	<0.001
HbA1c (%)	5.6 (0.6)	5.6 (0.6)	5.6 (0.9)	5.5 (0.5)	<0.001
FBG (mmol/L)	5.4 (1.0)	5.4 (1.2)	5.4 (1.1)	5.3 (0.9)	0.438

Continuous variables are presented as the means (SD).
PAL included four aspects: transportation activity, occupational activity, domestic activity and leisure activity.
Hypertension was defined as self-reports of a history of hypertension diagnosis, and/or systolic pressure ≥140 mm Hg, and/or diastolic pressure ≥90 mm Hg.
BMI, body mass index; FBG, Fasting blood-glucose; HbA1c, Glycosylated Hemoglobin ; MET-hour, metabolic equivalent hours; PAL, Physical activity level.

disrupts the expression of the clock gene.[9 11] Circadian rhythm closely regulates insulin secretion and sensitivity, and has strong effects on glucose metabolism, which have been confirmed in animal studies.[12–14] However, nowadays, little attention is paid to the importance of energy intake balance throughout the day in the onset of T2D, especially at breakfast and dinner.

It is worth noting that owing to dynamic changes in energy intake at breakfast and dinner over the course of a lifetime, the trend of energy intake level at dinner vs breakfast over time can genuinely reflect the individual's dietary status and may be more effective in verifying the relationship with T2D risk. Taking advantage of distinct trajectories can solve this challenge, and the association between energy consumption trajectories at dinner vs breakfast throughout the adult life course and T2D has not yet been reported.

In the present study, we used unique latent class trajectory modelling (LCTM) over 14 years with longitudinal data from the China Health and Nutrition Survey (CHNS) and provided several reasonable curves for energy consumption at dinner vs breakfast. It is necessary to establish this association to understand the relationship between energy intake at dinner versus breakfast and T2D by the dietary trajectories, which provides effective strategies for T2D prevention by dietary interventions.

METHODS

The China Health and Nutrition Survey

The CHNS, which is an ongoing, open, prospective cohort study and is conducted in 15 provinces and municipal cities in China, takes advantage of a multistage, random cluster process to draw a sample of about 7200 households with over 30 000 individuals and has already completed nine follow-ups from 1989 to 2011. According to the 2010 census, the provinces included in the CHNS sample constituted 47% of China's population in 2011.[15] Dietary intake assessment in CHNS involved three consecutive 24 hours dietary recalls for participating individuals and a household food inventory which involved the weighing and measuring of products (used to obtain information on edible oils and condiments consumption) over the same 3 days. Each participant provided written informed consent. To ensure the quality of the investigation, strict quality control procedures including data collection, data entry, data check and data clean were implemented throughout the investigation.

Study population

The current study sample included adults aged over 18 years in seven surveys from 1997 to 2011. By the end of 2011, there were 27 887 available participants across 41 724 observations in the CHNS for this study. Excluded

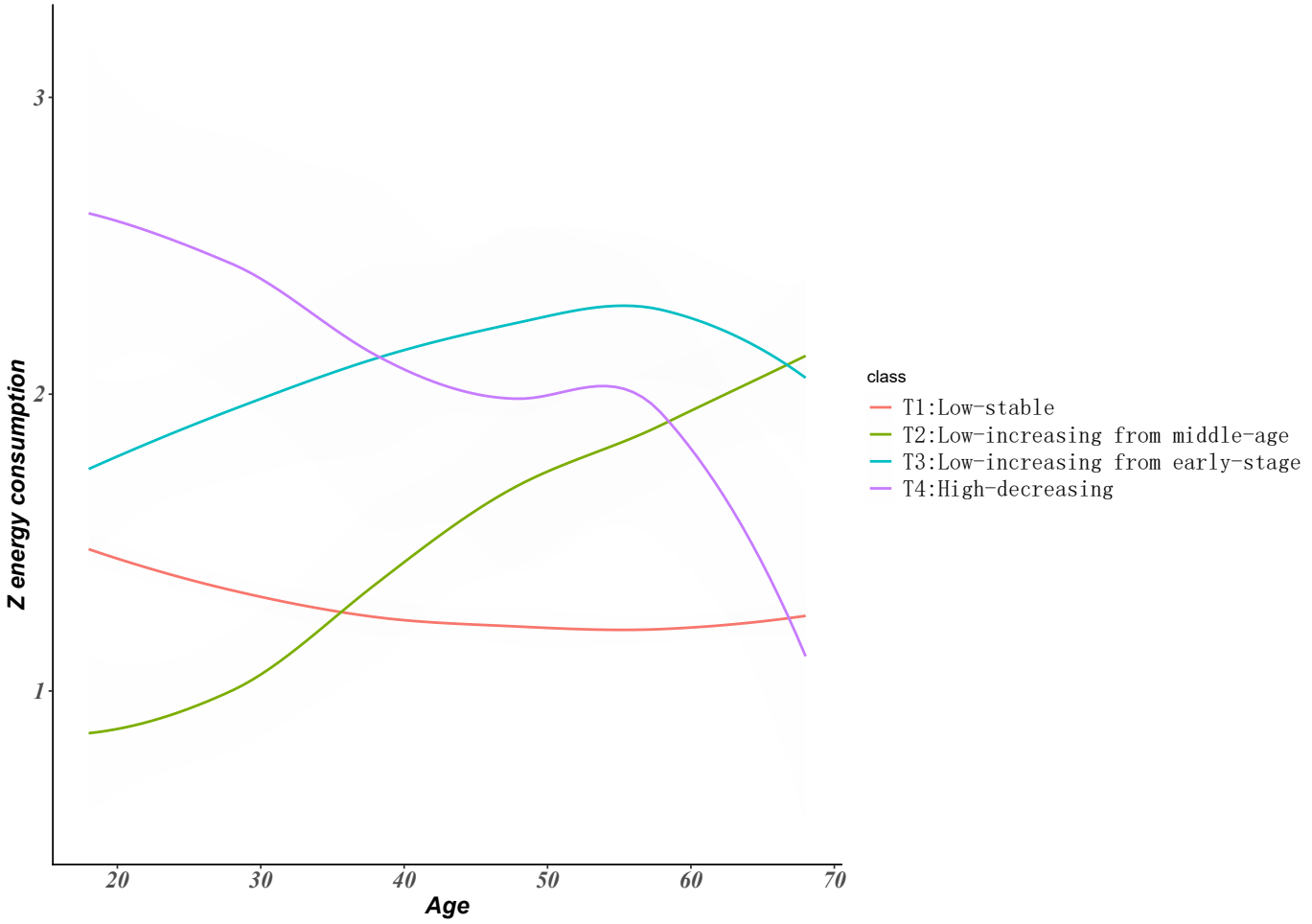

Figure 1 Trajectories of Z energy consumption in men and women (n=10, 727) from the CHNS by LCTM. CHNS, China Health and Nutrition Survey; LCTM, Latent class trajectory modelling.

were those less than 18 years old in the first survey (n=5686); participants with only one survey (n=8985); pregnant women (n=290); participants who were T2D patients in the first survey (n=327) and who had a total energy intake <500 kcal/day or >4500 kcal/day (n=1736). We further excluded 136 participants owing to missing breakfast or dinner data during follow-up. After these exclusions, the total subjects for our study included 10 727 adults (5488 women and 5239 men) who ranged from two to six measurement surveys (two visits, n=2792; three visits, n=1857; four visits, n=1942; five visits, n=2015; six visits, n=2121).

Questionnaire survey

A structured questionnaire was used by trained personnel, to collect information including demographic characteristics, dietary habits, lifestyle, physical activity and anthropometric indicators based on individuals, households and communities. In the CHNS, individual dietary intake for three consecutive days was collected for every household member, and an individual's energy and macronutrients intake in the meals was equal to the sum of individual survey section and household survey section. The latter, which contained energy and macronutrients in cooking oil and condiments, was equally distributed to individuals and in proportion to each meal. Energy and macronutrients were calculated by three versions of the Chinese food composition table (FCT). The 1991 FCT version was used in 1997 and 2000. The 2002/2004 (two books combined) FCT versions were used in 2004, 2006, 2009 and 2011. Current smoking was defined as a positive response to the question 'do you still smoke cigarettes now?' Participants who answered 'never smoked' to the question 'Have you ever smoked cigarettes (including hand-rolled or device-rolled)?' were classified as never smoked, and who had a positive answer to the questions 'Have you ever smoked cigarettes (including hand-rolled or device-rolled)?' and had a negative answer to 'do you still smoke cigarettes now?' as ex-smoker. The amount of alcohol consumed was measured by drinks and a standard drink was any drink that contained about 0.6 fluid ounces or 14 g of pure alcohol.[16] For this study, less than seven standard drinks/week was defined as light alcohol consumption, 7–21 standard drinks/week as moderate and more than 21 drinks/week as heavy.[17] Physical activity mainly contained four domains, namely, transportation activity, occupational activity, domestic activity and leisure activity.[18] The total

Table 2 Association between Z energy consumption at dinner vs breakfast trajectories and T2D by Cox regression models

Trajectory	Case/n*	Case (%)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
Low-stable (T1)	511/6,883	7.42	1	1	1	1
Low-increasing from middle age (T2)	119/1,425	8.35	1.07 (0.86 to 1.33)	1.08 (0.87 to 1.34)	1.08 (0.87 to 1.33)	1.04 (0.84 to 1.29)
Low-increasing from early stage (T3)	130/1,565	8.31	1.43 (1.16 to 1.76)	1.39 (1.13 to 1.72)	1.38 (1.12 to 1.71)	1.29 (1.04 to 1.60)
High decreasing (T4)	81/854	9.48	0.99 (0.72 to 1.37)	0.96 (0.70 to 1.33)	0.95 (0.69 to 1.32)	0.95 (0.68 to 1.31)
P trend			0.048	0.087	0.11	0.237

Model 1 was adjusted by age, sex and urban index.
Model 2 was further adjusted by smoking, drinking, education levels and physical activity.
Model 3 was further adjusted by total energy intake, protein intake, fat intake and carbohydrate intake.
Model 4 was adjusted by all variables in model 3, with further adjustment for the history of hypertension and BMI.
N=10 727.
*Number of type 2 diabetes cases/number of participants with this trajectory.
BMI, body mass index; T2D, type 2 diabetes.

number of hours/week in each activity for the metabolic equivalent of task, which represented the ratio of an individual's working metabolic rate relative to resting metabolic rate, was an indicator that accounted for the average intensity and the time spent in physical activity.[18] Hypertension was defined as persistent systolic blood pressure measurements of ≥140 mm of mercury (mm Hg) and/or 90 mm Hg of diastolic blood pressure. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres. Urbanicity was defined using a multidimensional 12-component urbanisation index capturing community-level physical, social, cultural and economic environments.

Outcome measures

The outcome of interest was T2D that was defined as a self-reported history of T2D, and/or fasting blood glucose ≥7.0 mmol/L and/or glycated haemoglobin ≥40 mmol/L (6.5%) in the 2009 survey, and/or receiving any of the following treatment methods, such as special diet, weight control, oral medicine, injection of insulin, Chinese traditional medicine and home remedies. There were 801 cases of T2D in this study.

Statistical analysis

All statistical analyses were performed using R V.3.5.3 (www.r-project.org/). A two-sided $p<0.05$ was considered statistically significant. The ratio dinner energy intake divided by breakfast energy intake (Z=dinner/breakfast) was normalised by Tukey transformation to improve the normality of the distribution and was used as an independent variable during the study. The continuous variables were described by mean±SD and the categorical variables by percentage. The missing covariables less than 5% were filled by multiple interpolation.

LCTM, which is a censored normal model, was used to identify Z energy consumption trajectories using the R package lcmm. We used statistically rigorous Bayesian information criteria to determine the best fit and each trajectory class included at least 3% of the sample population. When the trajectories were determined, it meant that a new nominal categorical variable was created and confirmed the trajectory classes of each participant. The new variable was further used in Cox multivariate regression models.

After the follow-up times of Non-T2D and T2D were calculated, Cox multivariate regression models, with age as the time scale, were used to estimate associations between trajectories of Z energy and risk of T2D. The HR and 95% CI were calculated. Models were adjusted for covariates including age, sex, smoking, drinking, physical activity, education level, urbanisation index, total dietary energy, fat, protein, carbohydrate, BMI and hypertension status.

However, blood samples from participants were collected only in 2009 in the CHNS. After participants were classified into different Z energy consumption trajectories, subgroup analyses were performed to determine

Table 3 Difference for T2D-related factors across Z energy consumption trajectories in men and women

Variables	T1	T2	T3	T4	P value
TG (mmol/L)	1.66 (1.39)	1.64 (1.39)	1.73 (1.49)	1.69 (1.57)	0.027
TC (mmol/L)	4.86 (0.98)	4.92 (1.03)	5.02 (1.04)	4.8 (0.94)	0.049
UA (µmol/L)	301.50 (98.94)	317.29 (113.82)	324.71 (107.39)	312.54 (111.57)	<0.001
ApoA (mmol/L)	1.17 (0.39)	1.14 (0.29)	1.17 (0.53)	1.12 (0.30)	0.070
ApoB (mmol/L)	0.92 (0.26)	0.92 (0.28)	0.94 (0.27)	0.89 (0.25)	0.023
hs-CRP (mmol/L)	2.5 (9.49)	2.57 (4.94)	2.42 (5.6)	2.13 (4.58)	0.399

Generalised linear model was used to probe for differences across different trajectories with adjustment for age, smoking, physical activity, education levels, urban index, hypertension statues and BMI. Data are mean (SD).
ApoA, apolipoprotein A; ApoB, apolipoprotein B; BMI, body mass index; FPG, fasting plasma glucose; hs-CRP, high sensitivity C reactive protein; TC, total cholesterol; T2D, type 2 diabetes; TG, triacylglycerol; UA, uric acid.

the relationship between obtained Z energy consumption trajectories and blood indicators adjusted with the above covariables by generalised linear models, which could recognise T2D-related blood indicators that were statistically different in different trajectories.

Based on the above, mediation analysis models were performed using the R package lavaan, to examine whether the association between Z energy consumption trajectories and risk of T2D was mediated by these biomarkers with adjustment for the above covariates.

Sensitivity analysis is an important method to verify the stability of the results and is an important part of statistical analysis in epidemiological studies. Six sets of sensitivity analyses were performed as follows: in set 1, we examined the relationship between the ratio of single-time point Z energy consumption and the risk of T2D, which would verify whether trajectory analysis could provide additional information; in set 2, the analysis was performed in men; in set 3, the analysis was performed in women; in set 4, the analysis was administered to overweight people; in set 5, breakfast and morning snack were treated as breakfast and the study was reanalysed; in set 6, based on the fifth sensitivity analysis, dinner and evening snack were treated as dinner.

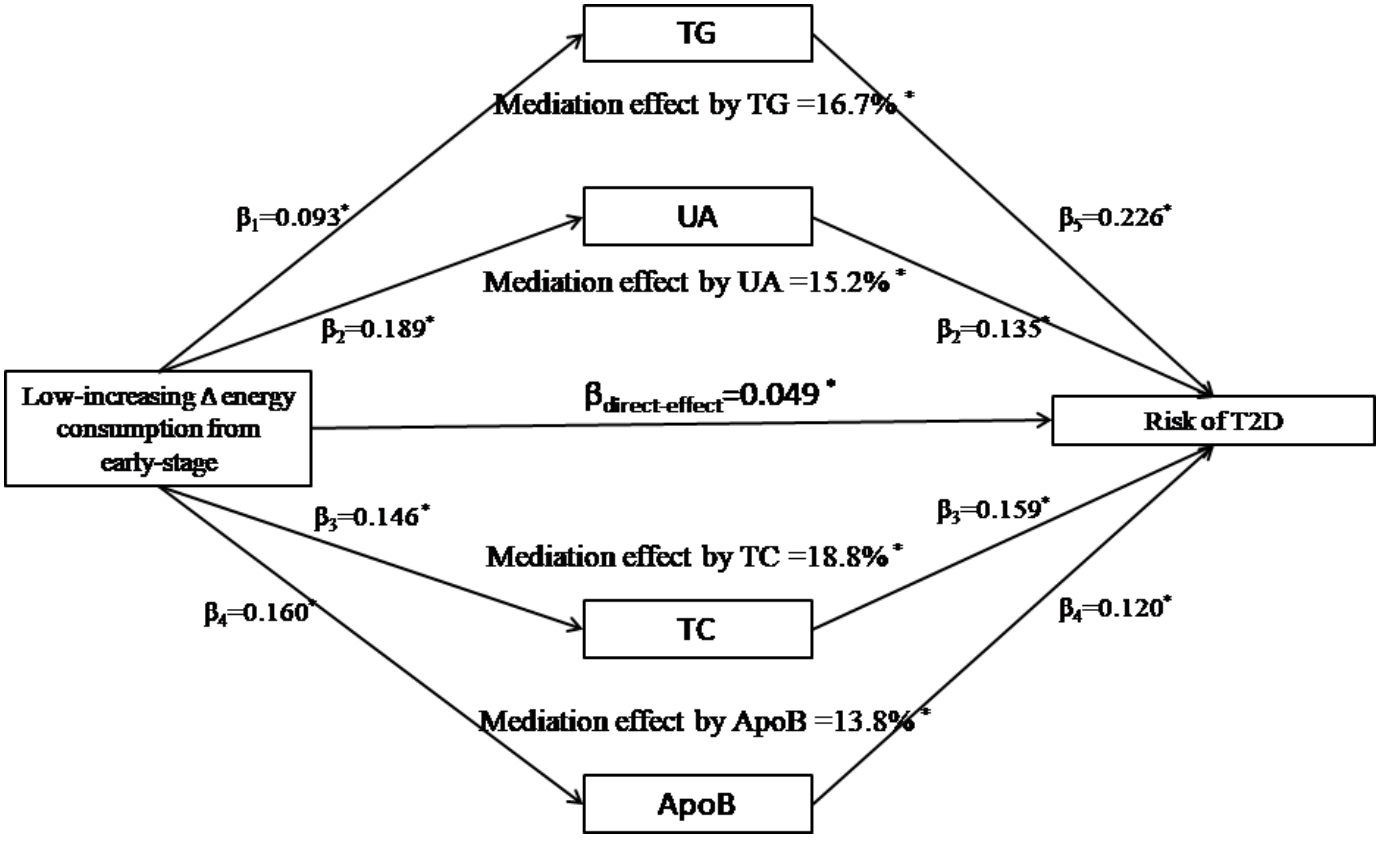

Figure 2 Mediation effects of triacylglycerol (TG), uric acid (UA), total cholesterol (TC) and apolipoprotein B (ApoB) on the association between Z energy consumption trajectories and risk of T2D. Data are standardised regression coefficients with adjustment for covariates; *p<0.05 for coefficients different from 0. T2D, type 2 diabetes.

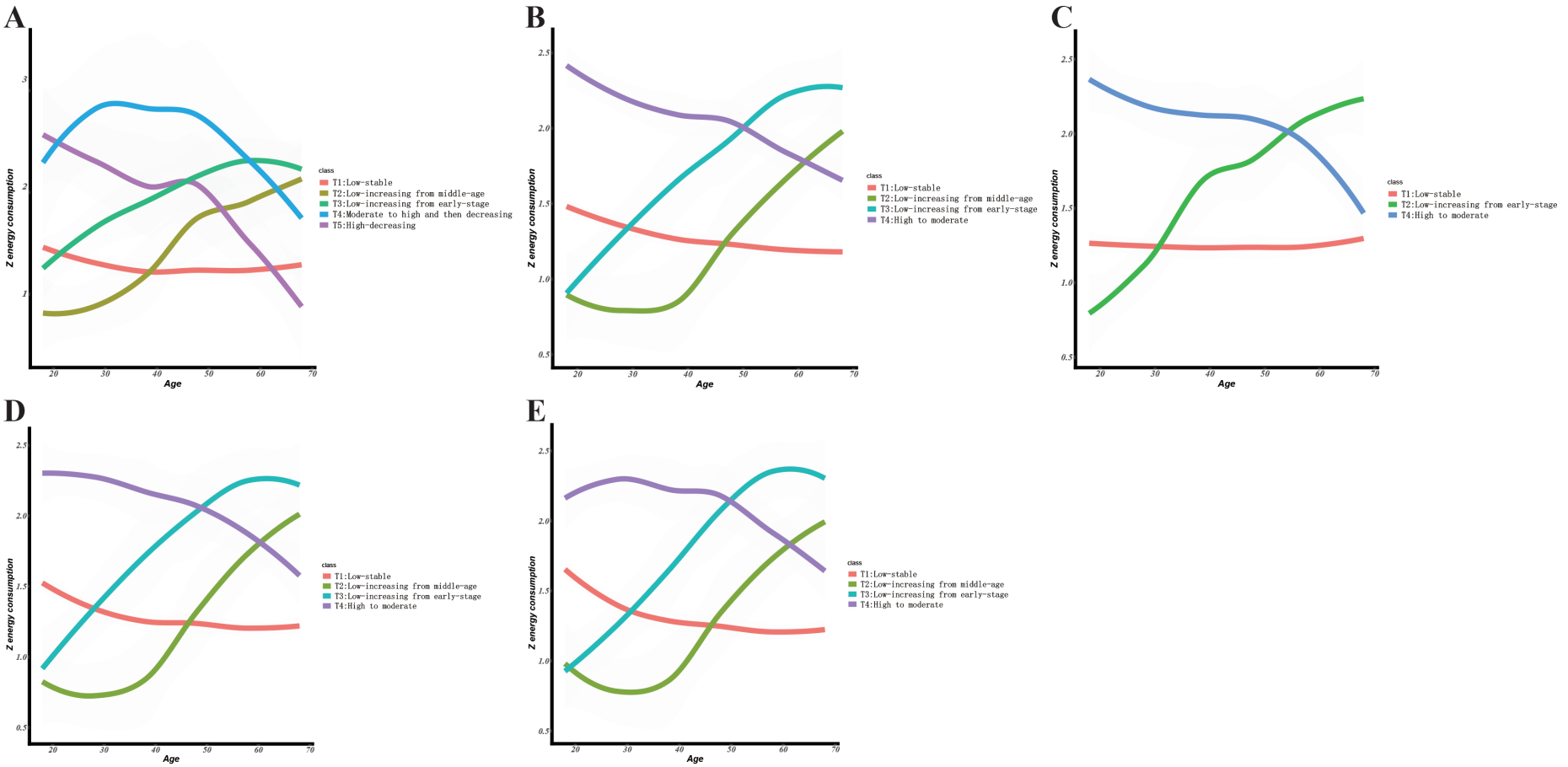

Figure 3 Trajectories of Z energy consumption in men (A, n=5239), women (B, n=5488) and overweight (C, n=3287) from the CHNS by LCTM, respectively. When breakfast and morning snack were served as breakfast, trajectories of Z energy consumption in men and women were shown in (D) (n=10727). When breakfast and morning snack were served as breakfast, and dinner and evening snack were served as dinner, trajectories of Z energy consumption in men and women were shown in (E) (n=10727) from the CHNS by LCTM. CHNS, China Health and Nutrition Survey; LCTM, latent class trajectory modelling.

Table 4 Association between Z energy consumption at dinner versus breakfast trajectories and T2D by Cox regression models in sensitivity analyses

Trajectory	Case/n*	Case (%)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)
Sensitivity analysis 1						
Low stable (T1)	249/3 to 375	7.38	1	1	1	1
Low increasing from middle age (T2)	20/343	5.83	0.64 (0.40 to 1.03)	0.64 (0.40 to 1.02)	0.64 (0.40 to 1.03)	0.64 (0.40 to 1.01)
Low increasing from early stage (T3)	70/777	4.92	1.46 (1.09 to 1.96)	1.39 (1.04 to 1.86)	1.38 (1.03 to 1.85)	1.35 (1.01 to 1.82)
Moderate to high and then decreasing (T4)	19/256	9.01	1.44 (0.89 to 2.32)	1.35 (0.84 to 2.19)	1.34 (0.83 to 2.17)	1.34 (0.83 to 2.18)
High decreasing (T5)	24/488	7.42	1.00 (0.66 to 1.53)	0.94 (0.62 to 1.44)	0.94 (0.61 to 1.43)	0.93 (0.61 to 1.43)
P trend			0.152	0.320	0.367	0.404
Sensitivity analysis 2						
Low stable (T1)	252/3 to 383	7.45	1	1	1	1
Low increasing from middle-age (T2)	23/284	8.10	0.82 (0.52 to 1.27)	0.82 (0.53 to 1.28)	0.82 (0.53 to 1.28)	0.81 (0.52 to 1.26)
Low increasing from early stage (T3)	93/1 to 164	7.99	1.35 (1.04 to 1.74)	1.33 (1.03 to 1.72)	1.32 (1.02 to 1.71)	1.36 (1.05 to 1.75)
High to moderate (T4)	51/657	7.76	0.99 (0.71 to 1.38)	0.98 (0.71 to 1.37)	0.98 (0.70 to 1.37)	1.00 (0.72 to 1.39)
P trend			0.038	0.048	0.054	0.036
Sensitivity analysis 3						
Low stable (T1)	310/2 to 431	12.75	1	1	1	1
Low increasing from early stage (T2)	90/706	12.75	1.33 (1.03 to 1.71)	1.30 (1.01 to 1.67)	1.29 (1.01 to 1.67)	1.29 (1.02 to 1.67)
High to moderate (T3)	29/150	19.33	0.82 (0.54 to 1.24)	0.83 (0.55 to 1.25)	0.82 (0.54 to 1.24)	0.83 (0.55 to 1.25)
P trend			0.047	0.078	0.076	0.078
Sensitivity analysis 4						
Low stable (T1)	535/7 to 308	7.32	1	1	1	1
Low increasing from middle age (T2)	27/394	6.85	0.63 (0.42 to 0.94)	0.65 (0.43 to 0.96)	0.64 (0.43 to 0.95)	0.69 (0.46 to 1.03)
Low increasing from early stage (T3)	140/1 to 853	7.56	1.39 (1.14 to 1.69)	1.35 (1.11 to 1.65)	1.36 (1.12 to 1.66)	1.28 (1.04 to 1.56)
High to moderate (T4)	99/1 to 172	8.45	1.14 (0.90 to 1.44)	1.13 (0.89 to 1.43)	1.12 (0.89 to 1.42)	1.10 (0.87 to 1.38)
P trend			0.001	0.003	0.003	0.020
Sensitivity analysis 5						
Low stable (T1)	497/6 to 645	7.48	1	1	1	1
Low increasing from middle age (T2)	34/511	6.85	0.68 (0.48 to 0.98)	0.70 (0.49 to 1.01)	0.70 (0.49 to 0.99)	0.70 (0.49 to 1.00)
Low increasing from early stage (T3)	180/2 to 441	7.37	1.27 (1.06 to 1.52)	1.23 (1.03 to 1.48)	1.25 (1.04 to 1.49)	1.22 (1.02 to 1.46)
High to moderate (T4)	90/1 to 130	7.96	1.01 (0.79 to 1.28)	1.00 (0.78 to 1.27)	1.00 (0.79 to 1.27)	0.99 (0.78 to 1.26)
P trend			0.014	0.034	0.028	0.053

Continued

Table 4 Continued

Trajectory	Case/n*	Case (%)	Model 1 HR (95% CI)	Model 2 HR (95% CI)	Model 3 HR (95% CI)	Model 4 HR (95% CI)

Model 1 was adjusted by age and urban index.
Model 2 was further adjusted by smoking, drinking, education levels and physical activity.
Model 3 was further adjusted by total energy intake, protein intake, fat intake and carbohydrate intake.
Model 4 was adjusted by all variables in model 3, with further adjustment for the history of hypertension and BMI.
*Number of type 2 diabetes cases/number of participants with this trajectory.
BMI, body mass index; T2D, type 2 diabetes.

Patient and public involvement

The patients or members of the public were not involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

Participant characteristics

Characteristics of the study population from the CHNS by survey years are presented in online supplemental material (table 1). Age and BMI showed increasing trends across survey years. However, total energy and total carbohydrate intake showed decreasing trends.

Trajectories of energy intake ratio at dinner versus breakfast

In this cohort of 10 727 Chinese adults, consumption trajectories of Z energy are shown in figure 1 and each trajectory group was named based on their visual patterns of changes in Z energy levels. In figure 1, the first trajectory, labelled 'T1: light stable,' corresponded to participants who maintained low Z energy throughout the survey period. The second trajectory, 'T2: low increasing from middle age,' corresponded to participants who experienced a rapid increase in Z energy level from middle age compared with T1. The third trajectory, 'T3: low increasing from early age,' corresponded to participants who experienced a rapid increase in Z energy level from early-age compared with T1. The fourth trajectory, 'T4: high decreasing,' corresponded to participants who started with heavy Z energy level and then declined with age. The trajectories from T1 to T4 were estimated to include 64.2%, 13.2%, 14.6% and 8.0% of participants, respectively.

Baseline characteristics by different trajectories of total energy intake ratio at dinner versus breakfast

Table 1 presents the baseline characteristics of study variables by different trajectories of Z energy consumption. Baseline drinking, total energy intake and total protein intake did not differ significantly across trajectories of Z energy. In contrast, age, BMI, smoking, physical activity, education levels, total fat or carbohydrate intake, energy intake at breakfast or dinner, urban index and hypertension status varied significantly across different trajectories of Z energy.

Association between energy intake ratio at dinner versus breakfast trajectories and risk of T2D

Associations between Z energy consumption trajectories and risk of T2D are presented in table 2. Compared with T1, the trajectory labelled 'T3' was significantly associated with increased risk of T2D (HR 1.29 (95% CI 1.04 to 1.60)) with adjustment for covariates.

Trajectories of total energy ratio at dinner versus breakfast and biomarkers of T2D

Differences for biomarkers across Z energy trajectories in men and women are shown in table 3. For Z energy, triacylglycerol (TG), total cholesterol (TC), uric acid (UA) and apolipoprotein B (ApoB) in the T3 trajectory were higher than the other three trajectory classes (T1, T2 and T4) (all

p<0.05). Apolipoprotein A and high sensitivity C reactive protein in the T3 trajectory showed non-significant higher trends than in the three other trajectory classes.

Mediation analysis

Figure 2 shows mediation effects of TG, TC, UA and ApoB on the association between Z energy trajectory (T3) and risk of T2D. The total effect of Z energy consumption trajectories was estimated at 13.8%. The β1 to β8 were used to calculate the overall indirect effect for four factors. The percentages of the total effect mediated by TG, UA, TC and ApoB were estimated at 16.7%, 15.2%, 18.8% and 13.8%, respectively.

Sensitivity analysis

Online supplemental table 2 shows the relationship between the ratio of single-time point Z energy consumption and T2D risk, and demonstrates that Z energy consumption was significantly associated with T2D risk only in 1997 (OR 1.55 (95% CI 1.19, 1.91)) with adjustment for covariates. In men, this study identified five distinct trajectories of change in dietary Z energy levels in figure 3A which are labelled 'T1: low stable,' 'T2: low increasing from middle age,' 'T3: low increasing from early stage,' 'T4: moderate to high and then decreasing' and 'T5: high decreasing.' The trajectories from T1 to T5 were estimated to include 64.5%, 6.5%, 14.8%, 4.9% and 9.3% of participants, respectively. Figure 3B demonstrats four distinct trajectories of changes in Z energy levels in women during six surveys, which are labelled 'T1: light stable,' 'T2: low increasing from middle age,' 'T3: low increasing from early age' and 'T4: high to moderate.' The trajectories from T1 to T4 were estimated to include 61.6%, 5.2%, 21.2% and 12.0% of participants, respectively. In the overweight population, this study identified three distinct trajectories of change in dietary Z energy levels in figure 3C, which were labelled 'T1: low stable,' 'T2: low increasing from early stage,' and 'T3: high to moderate.' The trajectories from T1 to T3 were estimated to include 74.0%, 21.4% and 4.6%, respectively. In the fifth and sixth sets of sensitivity analyses, this study identified four distinct trajectories of change in dietary Z energy levels, which are presented in figure 3D,E, and labelled 'T1: low stable,' 'T2: low increasing from middle stage,' 'T3: low increasing from early stage' and 'T4: high to moderate.' The trajectories from T1 to T4 were estimated to include 68.1%, 3.7%, 17.2% and 10.9% in the fifth set of sensitivity analysis and 61.9%, 4.7%, 22.7% and 10.5% in the sixth set of sensitivity analysis, respectively.

Association between dietary Z energy trajectories and the risk of T2D in the second to sixth sets of sensitivity analyses were similar to the results above and the results are shown in table 4. Compared with low stable, trajectories labelled 'T4'was significantly associated with increased risk of diabetes (HR 1.35 (95% CI 1.01 to 1.81)) in men; trajectories labelled 'T3' HR 1.36 (95% CI 1.05 to 1.75) in women; trajectories labelled 'T2' HR 1.29 (95% CI 1.02 to 1.67) in the overweight population; trajectories labelled 'T3' HR 1.28 (95% CI 1.04 to 1.56) in the fifth set of sensitivity analysis; trajectories labelled 'T3' HR 1.22 (95% CI 1.02 to 1.46) in the sixth set of sensitivity analysis.

DISCUSSION

In this prospective cohort of Chinese adults with six surveys, we identified four distinct Z energy consumption trajectories in which the low increasing from early-stage trajectory group was significantly associated with increased risk of T2D and this trajectory had higher TG, TC, UA and ApoB than other trajectories. Furthermore, TG, TC, UA and ApoB partially mediated the association between trajectory and T2D.

The low increasing from early-stage trajectory group for Z energy consumption demonstrated that participants gradually increased Z energy consumption from early stage. In a large longitudinal study, an increased percentage of daily energy consumed at breakfast was associated with relatively lower weight gain,[19] and being overweight was associated with increased glucose intolerance and T2D risk.[20] Above all, these studies partially supported our observations and are consistent with our results.

The alteration of circadian patterns might be another mechanism to explain our observations. The effects of diet on circadian rhythmicity had already shown that chrononutrition could contribute to circadian perturbance and influence the manifestation of metabolic disorders such as T2D.[10] Current evidence suggests that the time of day in which the amount of calories is consumed can affect glycaemic control. Animal studies showed that with the same total daily energy intake, low-caloric breakfast along with high-caloric dinner, which could impair peripheral clock gene expressions, resulted in higher daily glucose excursions.[11 21] Taken together, our findings are consistent with other studies that explained the impact of a low energy intake at breakfast and a high energy intake at dinner for T2D risk.

The difference for T2D-related factors across different Z energy consumption trajectories indicated that the low increasing from early-stage trajectory group for Z energy in which the proportion of Z energy still had been a relatively high level, was probably associated with higher TG, TC, UA and ApoB in later adulthood. Further, TG, TC, UA and ApoB partially mediated the association between trajectory and T2D, suggesting that gradually increasing Z energy consumption in the early stage was associated with increased risk of T2D partially through increasing TG, TC, UA and ApoB. Human blood lipid levels had diurnal variations and lipid metabolism involved multiple organs and tissues which were regulated by circadian rhythm genes.[4 5 22] Animal models demonstrated that lipoprotein lipase activity was higher at 19:00 hours than in the morning. Previous studies have shown that elevated levels of total and low-density lipoprotein cholesterol were associated with energy intake at night based on a representative sample of adults in Taiwan.[23] Meanwhile, meal intake earlier in the day for 2 weeks caused a significant decrease

in serum TG.[24] Microsomal triglyceride transfer protein, which is involved in ApoB lipoproteins' synthesis in liver and in intestine, had higher activity from afternoon to night.[23] However, permanent or temporary, hypercaemic or hypouricaemic states, was a simple measurable marker of derangements in energy utilisation of circadian or intermediate metabolism.[25–28] Both hypertriacylglycerolaemia and hyperuricaemia have been reported to be associated with T2D through inducing insulin resistance and beta cells' dysfunction as described in previous studies.[29 30] A cross-sectional study showed that patients with T2D had higher TC and ApoB than participants without diabetes.[31] To sum up, our study showed previous research and explained that TG, TC, UA, and ApoB partially mediated the association between trajectory and T2D risk.

In addition, in the process of studying between Z energy trajectories and the risk of T2D, low increasing from middle age (T2 trajectory) and high decreasing (T4 trajectory) were not associated with risk of T2D compared with light stable (T1 trajectory). Although the T2 trajectory was always rising, it was always lower than the T3 trajectory and began to rise from middle age compared with the T1 trajectory, and the T2 trajectory was higher than the T3 trajectory only in late adulthood, which might be the reason that we did not observe an increasing risk of T2D. The T4 trajectory was at a high level in early adulthood which could have caused changes in circadian rhythms. However, the circadian rhythm was an adjusted factor and was reset by food intake. Therefore, when the T4 trajectory went down, the master clock could be phase adjusted.

This study was the first on this subject area conducted in an Asian population with a relatively large cohort size and long follow-up duration. However, we also recognised that there were several limitations to our study. First, during the diet survey, 3 days' worth of detailed household food consumption information was collected. In addition, individual dietary intake for three consecutive days was collected for every household member through the questionnaire. However, the respondents might have misreported the amount and types of food intake, resulting in inaccurate values for energy and macronutrition measurement in three consecutive days. Second, the diagnosis of T2D was mainly based on self-report and blood samples used in the 2009 survey, which led to the incidence of T2D lower in this study than the national norm level and might bias the results. Third, this study included only Asian participants, which was likely to limit the generalisability of our findings to other ethnic populations. Lastly, it was limited by the possibility of residual confounding, the presence of which would affect the accuracy of estimates in this study. There are several strengths in this study. First, the CHNS database, which is a database with high quality and integrity, and which is a representative database of Chinese in diet surveys, includes 15 provinces and municipal cities which represented 47% of the Chinese population based on the 2010 census. Second, using a single time point to detect the association between Z energy and the risk of T2D, we did not observe a positive association in each survey, which highlighted the importance of taking advantage of LCTM to study the relationship between Z energy and the risk of T2D and showed the application value of our research.

In conclusion, this study emphasised the harmful effect of a gradual increase in Zenergy consumption from an early stage on the development of T2D and partially mediated by TG, TC, UA and ApoB, highlighting that it was necessary to intake more energy at breakfast to prevent T2D in adults. Additional studies are needed to evaluate the low increasing from middle age or high-decreasing trajectory of Z energy intake.

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Competing interests None declared.

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