

# Habitually skipping breakfast is associated with chronic inflammation: a cross-sectional study

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#### **Abstract**

Objective: We examined whether breakfast frequency was associated with chronic inflammatory, as assessed by high-sensitivity C-reactive protein (CRP) concentration.

Design: Cross-sectional study.

Setting: Kailuan community, China.

*Participants:* Included were 70 092 Chinese adults without CVD and cancer in 2014 with CRP concentrations <10 mg/l, when breakfast frequency was assessed via a questionnaire, and plasma CRP concentration was measured.

Results: Breakfast frequency was associated with CRP concentration (*P*-trend < 0.001). The adjusted mean CRP was 1.33 mg/l (95 % CI 1.23, 1.44) for the 'no breakfast' group and 1.07 mg/l (95 % CI 1.0, 1.14) for the 'breakfast everyday' group (*P*-difference < 0.001), adjusting for age, sex, diet quality, total energy, obesity, education, occupation, marital status, smoking, alcohol consumption, blood pressure, sleep parameters, fasting blood glucose and lipid profiles. Consistently, the adjusted OR for CRP  $\geq$  1.0 mg/l and CRP  $\geq$  3.0 mg/l were 1.86 (95 % CI 1.73, 2.00) and 1.27 (95 % CI 1.15, 1.40), respectively, when comparing these two breakfast consumption groups (*P*-trend < 0.001 for both). The associations were more pronounced among older adults, relative to those who were younger (*P*-interaction < 0.001). Significant association between breakfast skipping and elevated CRP concentration was observed in those with poor diet quality, but not those with good diet quality.

*Conclusions*: Habitually skipping breakfast is associated with elevated concentrations of CRP. Future prospective studies including repeated assessment of inflammatory biomarkers and a collection of detailed information on type and amount of breakfast foods are warranted.

Keywords
Breakfast consumption
Chronic inflammation
C-reactive protein
Cardiovascular health

The emphasis on breakfast eating for overall health can be traced back to the 16th century in Europe<sup>(1)</sup>. Described as the most important meal of the day, breakfast provides nutrients for the body after overnight fasting<sup>(2)</sup>. Recently, several studies demonstrate that breakfast skippers may have a higher risk of developing diabetes<sup>(3)</sup>, hypertension<sup>(4)</sup>, CVD<sup>(5,6)</sup> and cancer<sup>(7)</sup>, relative to breakfast eaters. Of note, all of the aforementioned chronic conditions or diseases are associated with chronic inflammation<sup>(6,8–10)</sup>. Two recent cross-sectional studies

reported that consumption of breakfast foods was associated with lower inflammation, assessed via serum C-reactive protein  $(CRP)^{(11)}$  or glycoprotein acetyls<sup>(12)</sup>. However, these studies were limited by an indirect assessment of breakfast consumption<sup>(11)</sup> or a small sample size  $(n 644)^{(12)}$ . The study by di Giuseppe *et al.*<sup>(11)</sup> assessed participants' breakfast consumption by determining whether they reported consumption of foods which were considered 'typical Italian breakfast foods' (e.g. milk, coffee, crisp bread and breakfast cereals). This assessment

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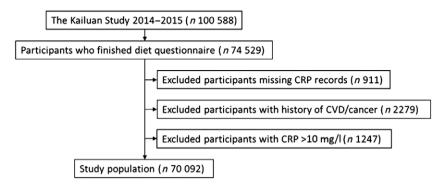


Fig. 1 Flow chart of participant inclusion. CRP, C-reactive protein

method is limited by the uncertainty on whether those 'typical Italian breakfast foods' were also eaten at lunch or dinner, other than breakfast.

Thus, we conducted a cross-sectional study to examine whether breakfast consumption frequency was associated with inflammatory status among 70 092 Chinese adults, after adjustment for overall dietary quality, sleep parameters, medical history, blood lipid profile and other potential confounders. Chronic inflammation, measured via plasma or serum CRP, is an accepted risk factor for many common conditions, including CVD<sup>(13)</sup>, type 2 diabetes<sup>(14)</sup> and hypertension<sup>(15)</sup>. The link between CRP and CVD is well established, while risk estimates vary slightly, even after adjusting for age, ethnicity, sex and other CVD risk factors. Since 2003, the Centers for Disease Control and Prevention and the American Heart Association (AHA) have recommended that CRP concentrations in the blood be quantified 'as an adjunct' to the traditional CVD risk factors (e.g. total cholesterol, HDL-cholesterol and systolic and diastolic blood pressure)(16). However, even in the absence of hyperlipidaemia, CRP has proven to be an effective indicator of CVD risk(6).

Upon existing evidences as aforementioned, regular breakfast consumption has been associated with reduced risk of chronic diseases, such as CVD. To understand the potential mechanism underlying this relationship, we aim to examine whether breakfast frequency was associated with inflammatory status, as assessed by high-sensitivity CRP concentration, among individuals who were free of CVD and cancer.

#### **Methods**

# Study population

The current study was based on two large cohorts: the Kailuan I study and the Kailuan II study, which have been described previously<sup>(17,18)</sup>. In brief, Kailuan I is a population-based prospective cohort launched in Tangshan City, China, in 2006, with 101 510 Chinese adults aged 18 years or older who lived in the Kailuan community. Kailuan II was launched in 2008 and includes 35 856 participants living

in the same community, who were not enrolled in the Kailuan I study. All participants of the Kailuan studies have undergone routine assessments, including physical examination, anthropometry and laboratory measures, at baseline. Biennial follow-ups were conducted to update information on lifestyle and health status. Information on habitual dietary intakes was assessed with a semi-quantitative FFQ in 2014. Among 74 529 participants who finished the FFQ, 911 were excluded due to missing CRP values, 2279 were excluded due to history of CVD or cancer and 1247 were excluded with clinical CRP concentrations >10 mg/l at the study visit (Fig. 1). Thus, the current study was based on 70 092 participants (57 631 men and 12 458 women; average age  $52 \pm 14$  years).

## Assessment of breakfast frequency

Breakfast frequency was assessed using the question 'how many days do you usually consume breakfast in a typical week?'. The possible answers were 'no breakfast', '1–2 times weekly', '3–5 times weekly' and 'breakfast every day'. Participants were then categorised into four groups based on their responses.

### Assessment of C-reactive protein concentration

Fasting (8–12 h) venous blood samples were drawn from the participants by nurses and transfused into vacuum tubes containing EDTA during the study visit. Following collection, all blood samples were analysed the same day in the Central Laboratory of Kailuan General Hospital. Plasma CRP concentration was measured using a high-sensitivity, particle-enhanced immunonephelometry assay (Cias Latex CRP-H; Kanto Chemical Co. Inc.) with a lower limit of detection of 0·1 mg/l. The intra-assay CV was 6·53 %, and the inter-assay CV was 4·78 %. Further details regarding the assessment of plasma CRP can be found elsewhere<sup>(19)</sup>.

We used two cut-off points for high CRP concentration based on its clinical relevance to CVD risk, as recommended by Centers for Disease Control and Prevention and AHA<sup>(16)</sup>:  $\geq 1.0$  mg/l (moderate-to-high CVD risk group) and  $\geq 3$  mg/l (high CVD risk group).





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## Assessment of covariates

Dietary data were collected with a validated semiquantitative FFO in 2014<sup>(20,21)</sup>. The semi-quantitative FFO includes thirty-three food items and seven condiments and asks how often the participants consumed each food item over the preceding year, with the options of never, daily, weekly or monthly. The consumption amount of each food was also assessed via the FFQ in the unit of liangs (50 g/liang). Diet quality was assessed by adherence to AHA recommendation (referred to as 'AHA diet score' in the current study), which was calculated based on the following five components: the consumption of fruits and vegetables, fish, Na, sweets, sugar-sweetened beverages and whole grains, as described previously. The score ranges from 0 (worst) to 5 (best)<sup>(20)</sup>.

During the study visit, weight and height were measured, and BMI was calculated as weight (kg)/height (m<sup>2</sup>). Systolic blood pressure was measured twice after participants were seated statically and averaged for further analysis<sup>(17)</sup>. An autoanalyser (Hitachi 747; Hitachi) was used to measure blood glucose, HDL-cholesterol and LDL-cholesterol, as detailed previously<sup>(20,22)</sup>.

Questionnaires were used to collect information on age, sex, lifestyle (smoking status, alcohol consumption and physical activity), medication use history (the use of antihypertensive drugs and/or antidiabetic drugs) and sociodemographic data (education level, marital status and occupation type)(20). Diabetic status was determined by fasting blood glucose > 7.0 mmol/l or the use of antidiabetic drug. Smoking status was divided into three categories: never, former and current. Alcohol consumption was divided into four categories: never, former, current <1 drink/d and current >1 drink/d. Physical activity level was assessed with the validated International Physical Activity Questionnaire, short version, and participants were categorised as inactive, moderately active or vigorously active<sup>(23)</sup>. Insomnia status was assessed using a Chinese version of the Athens Insomnia Scale (24,25). Questions included self-reported usual total hours of actual sleep at night and self-reported snoring + self-reported breathing stops<sup>(25)</sup>.

## Statistical analysis

Data were analysed with SAS version 9.4 (SAS Institute, Inc.). All statistical tests were two-sided. We used generalised linear models to calculate adjusted means and 95 % CI for CRP concentration. Because the distribution of CRP concentration was highly skewed, log-transformed CRP was used in the statistical analysis as the outcome variable in three models. In the models, we log-transformed CRP to better normalise the distribution. We then transformed back CRP measurements to exponential form to show clinically meaningful values to provide a clearer interpretation in the result section. Model 1 adjusted for age, sex and total

energy intake. Model 2 further adjusted for diet score, BMI, education level, occupation type, marital status, smoking status, alcohol use, sleep duration, insomnia, snoring and physical activity. Model 3 adjusted for the covariates in model 2 with the addition of the use of antihypertensive and antidiabetic drugs, systolic blood pressure, fasting blood glucose, LDL-cholesterol and HDL-cholesterol. A secondary sensitivity analysis was performed in addition to the three models to exclude participants with diabetes. Least squares means and corresponding CI were then transformed back to the standard CRP units. Trend test was performed by treating breakfast frequency as a continuous variable in the regression model. We tested multiplicative interactions between breakfast pattern and age, sex, BMI and the AHA diet score, in relation to CRP concentration, after adjusting for covariates in model 3.

To further assess the association between breakfast frequency and inflammatory status, we categorised participants according to their serum CRP concentration. Two cut-off points were used. Participants with CRP  $\geq 1.0 \text{ mg/l}$ were identified as at moderate risk of developing CVD and those with CRP  $\geq 3.0$  mg/l were at high risk of developing CVD<sup>(16)</sup>. Logistic regression was used to calculate OR and 95 % CI for increased inflammation (CRP) across different breakfast frequency groups.

#### Results

Among the 70 092 participants in the current study, 86 % reported breakfast consumption every day and 8% reported no breakfast (Table 1).

Compared with the 'breakfast everyday' group, individuals who skipped breakfaster at least 1 d (referred to as 'breakfast skippers' in the current study) were more likely to be men and younger in age and had higher education levels and total energy intake (Table 1).

CRP concentration was significantly higher among individuals in the 'no breakfast' group, relative to those who consumed breakfast every day (adjusted mean 1.33 v. 1.07 mg/l; P-trend < 0.001), after adjusting for age, sex, total energy intake, diet quality score, BMI, education level, occupation type, marital status, smoking status, alcohol use, physical activity, sleep parameters, blood pressure, fasting glucose concentration, antihypertensive drug use, antidiabetic drug use and lipid profiles (Table 2). Further, not eating breakfast increased the odds of elevated CRP. The adjusted OR, for the 'no breakfast' group v. the 'breakfast everyday' group, were 1.86 (95% CI 1.73, 2.00) for  $CRP \ge 1.0 \text{ mg/l}$  and 1.27 (95% CI 1.15, 1.40) for  $CRP \ge 3.0 \text{ mg/l}$  (*P*-trend < 0.001 for both; Table 3).

Age and diet quality significantly modified the associations between breakfast frequency and CRP (P for interaction < 0.001 for both; Table 4). The associations were more pronounced among older adults, relative to younger adults (P for interaction < 0.001). Interestingly, significant



Table 1 Baseline characteristics by breakfast consumption frequency

	Breakfast everyday (n 60 080)			3–5 breakfast/week (n2737)				t/week	No breakfast ( <i>n</i> 5813)			
	Mean		SD	Mean		SD	Mean		SD	Mean		SD
Age (years)	53.0		13.9	44.4		13.8	41.7		12.6	45.7		14.7
Male (%)		80.8			87.9			92.5			92.3	
College or above (%)		12.5			28.7			18.5			16.5	
Manual labour (%)		87.4			77·1			83.2			84.0	
Married (%)		87.3			87⋅1			85.9			94.4	
Current smoker (%)		44.6			53.2			56-1			37.8	
Current drinker (%)		40.2			55.1			55.6			22.7	
Antihypertensive drug (%)		13.4			9.0			9.4			11.9	
Antidiabetic drug (%)		3.9			2.3			2.3			3.0	
Physical exercises (%)		22.0			35.5			32.2			21.7	
Sleep duration (h)	7.93		1.37	7.85		1.67	7.99		1.81	8.14		2.10
Insomnia (%)		3.0			6.3			5.7			2.1	
Frequent snore (%)		12.9			22.8			14.4			5.9	
Total energy intake (kJ/d)	7150		2343	7427		2741	7464		2774	7565		2987
Diet quality score	1.47		0.89	1.51		0.84	1.61		0.89	1.29		0.67
BMI (kg/m²)	24.9		3.3	24.7		3.6	24.7		3.3	24.8		3.4
SBP (mmHg)	136		20	131		17	130		16	133		18
FBG (mmol/l)	5.82		1.69	5.63		1.42	5.59		1.51	5.70		1.37
LDL-cholesterol (mmol/l)	2.97		0.83	2.94		0.83	2.93		0.81	3.06		0.70
HDL-cholesterol (mmol/l)	1.36		0.41	1.36		0.35	1.36		0.33	1.44		0.43
CRP (mg/l)*	0.79		3.35	0.91		3.13	0.84		3.18	1.27		2.66

SBP, systolic blood pressure; CRP, C-reactive protein; FBG, fasting blood glucose. \*Genomic mean.

Table 2 Adjusted means and 95 % CI of C-reactive protein concentration, by breakfast consumption frequency

	Breakfast everyday (n 60 080)		3–5 breakfasts/week (n2737)			akfasts/week 11462)	No brea		
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	P for trend
Model 1	0.75	0.74, 0.76	0.83	0.79, 0.87*	0.74	0.7, 0.79	1.19	1.14, 1.23*	<0.001
Model 2 Model 3	1⋅22 1⋅07	1·14, 1·31 1, 1·14	1⋅31 1⋅14	1·22, 1·42* 1·05, 1·23*	1⋅18 1⋅01	1·07, 1·29 0·92, 1·1	1.55 1.33	1·43, 1·68* 1·23, 1·44*	<0.001 <0.001

Model 1 adjusted for age (years), sex and total energy intake (kJ/d).

Model 2 adjusted for age (years), sex, total energy intake (kJ/d), American Heart Association diet score, BMI (kg/m²), education level (elementary school, high school or college or above), occupation type (coal miner, other blue-collar jobs or other), marital status (single or married), smoking status (never, former or current), alcohol use (never, former, current <1 drink/d and current >1 drinks/d), sleep duration (<6, 6–7, 7–8 or  $\geq$ 8 h/d), insomnia (yes/no), snoring (never/rare, occasional or frequent) and physical activity (inactive, moderately active or vigorously active).

Model 3 adjusted for age, sex, total energy intake (kJ/d), American Heart Association diet score, BMI, education level (elementary school, high school or college or above), occupation type (coal miner, other blue-collar jobs or other), marital status, smoking status (never, former or current), alcohol use (never, former, current <1 drink/d and current >1 drinks/d), antihypertensive drug, antidiabetic drug, sleep duration (<6, 6–7, 7–8 or ≥8 h/d), insomnia (yes/no), snoring (never/rare, occasional or frequent) and physical activity (inactive, moderately active or vigorously active), systolic blood pressure (mmHg), fasting blood glucose status ('normal' (< 100 mmol/l), 'impaired fasting glucose' (100–125 mmol/l) or 'Diabetes' (>126 mmol/l or use of hypoglycaemic treatment)), LDL-cholesterol and HDL-cholesterol (mmol/l).

P values for difference from 'breakfast everyday' group are indicated as \* <0.05, \*\* <0.01,\*\*\* <0.001.\*\*\*

association between breakfast skipping and elevated CRP concentration was only observed in those with poor diet quality score, rather than those with a healthy diet quality (P for interaction < 0.001).

With the exclusion of participants with diabetes, adjusted means of CRP concentration were still significantly higher in 'no breakfast' group as compared with 'breakfast everyday' groups  $(1.26\ v.\ 1\ mg/l;\ P<0.001)$  (see online supplementary material, Supplemental Table).

#### Discussion

In this large-scale community-based study, we found that individuals who consumed no breakfast had a higher plasma CRP concentration, compared with those who consumed breakfast every day. This association was independent of demographic, anthropometric, socioeconomic and dietary variables. Elevated inflammation, measured via CRP<sup>(26)</sup>, is consistently associated with increased relative





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Table 3 OR and 95 % CI for high C-reactive protein (CRP), across breakfast frequency groups

	Breakfast everyday (n 60 080)			3–5 breakfasts/week (n2737)		1–2 breakfasts/week ( <i>n</i> 1462)			No breakfast (n 5813)				
	Mean		95% CI	Mean		95% CI	Mean		95% CI	Mean		95% CI	P for trend
CRP ≥ 1.0 mg/l													
Event,													
n		27 132			1474			755			4191		
%		45.2			53.9			51.6			72.1		
Model 1	1.00		Ref	1.26		1.16, 1.36	1.08		0.97, 1.20	2.66		2.49, 2.84	<0.001
Model 2	1.00		Ref	1.14		1.05, 1.10	0.99		0.88, 1.10	1.90		1.77, 2.05	<0.001
Model 3	1.00		Ref	1.15		1.06, 1.25	0.97		0.87, 1.08	1.86		1.73, 2.00	<0.001
$CRP \ge 3.0 \text{ mg/l}$						,			•			,	
Event													
n		8663			365			185			923		
%		14.4			13.3			12.7			15.9		
Model 1	1.00		Ref	0.94		0.83, 1.06	0.92		0.78, 1.09	1.53		1.41, 1.66	<0.001
Model 2	1.00		Ref	0.86		0.77, 0.97	0.88		0.74, 1.03	1.28		1.17, 1.41	<0.001
Model 3	1.00		Ref	0.87		0.77, 0.98	0.86		0.73, 1.02	1.27		1.15, 1.40	<0.001

Model 1 adjusted for age (years), sex and total energy intake (kJ/d).

Model 2 adjusted for age(years), sex, total energy intake (kJ/d), diet score, BMI (kg/m²), education level (elementary school, high school or college or above), occupation type (coal miner, other blue-collar jobs or other), marital status (single or married), smoking status (never, former or current), alcohol use (never, former, current <1 drink/d and current >1 drinks/d), sleep duration (<6, 6–7, 7–8 or  $\geq$ 8 h/d), insomnia (yes/no), snoring (never/rare, occasional or frequent) and physical activity (inactive, moderately active or vigorously active).

Model 3 adjusted for age (years), sex, total energy intake (kJ/d), diet score, BMI (kg/m²), education level (elementary school, high school or college or above), occupation type (coal miner, other blue-collar jobs or other), marital status, smoking status (never, former or current), alcohol use (never, former, current <1 drink/d), antihypertensive drug, antidiabetic drug, sleep duration (<6, 6–7, 7–8 or  $\geq$ 8 h/d), insomnia (yes/no), snoring (never/rare, occasional or frequent), physical activity (inactive, moderately active or vigorously active), systolic blood pressure (mmHg), fasting blood glucose status ('normal' (< 100 mmol/l), 'impaired fasting glucose' (100–125 mmol/l) or Use of hypoglycaemic treatment)), LDL-cholesterol and HDL-cholesterol (mmol/l).

Table 4 Adjusted means and 95 % CI of C-reactive protein concentration, by breakfast frequency, stratified by age, sex and diet quality score

		Breakfast everyday		3–5 breakfasts/ week		1–2 breakfasts/ week		No breakfast			
Interaction	n	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	P for trend	P for interaction
Age (years)											<0.001
<53 <sup>′</sup>	36 005	0.99	0.90, 1.09	0.99	0.89, 1.11	0.97	0.87, 1.09	1.15	1.03, 1.28*	<0.001	
≥53	34 087	1.53	1.35, 1.73	1.96	1.69, 2.28*	1.26	1.04, 1.53*	2.25	1.94, 2.62*	<0.001	
Sex											0.19
Women	12 458	1.08	0.90, 1.29	1.07	0.86, 1.32	1.03	0.78, 1.35	1.21	1.01, 1.58*	0.32	
Men	57 631	1.06	0.98, 1.15	1.15	1.05, 1.26*	1.01	0.92, 1.12	1.35	1.23, 1.47*	<0.001	
Diet quality score											<0.001
0–1	44 867	0.9	0.84, 0.96	0.91	0.84, 1	0.86	0.77, 0.96	1.2	1.1, 1.3*	<0.001	
2–5	25 225	0.76	0.67, 0.86	0.85	0.74, 0.98*	0.71	0.61, 0.83	0.76	0.66, 0.87	0.6	

Adjusted for age (years), sex, total energy intake (kJ/d), American Heart Association diet score, BMI (kg/m²), education level (elementary school, high school or college or above), occupation type (coal miner, other blue-collar jobs or other), marital status, smoking status (never, former or current), alcohol use (never, former, current <1 drink/d and current >1 drinks/d), antihypertensive drug, antidiabetic drug, sleep duration (<6, 6-7, 7-8 or ≥8 h/d), insomnia (yes/no), snoring (never/rare, occasional or frequent), physical activity (inactive, moderately active or vigorously active), systolic blood pressure (mmHg), fasting blood glucose status ('normal' (<100 mmol/l), 'impaired fasting glucose' (100–125 mmol/l) or 'Diabetes' (>126 mmol/l or use of hypoglycaemic treatment)), LDL-cholesterol and HDL-cholesterol (mmol/l).
\*P value for difference from 'breakfast everyday' group is indicated as <0.05.

risk of CVD<sup>(13,27)</sup> and has more recently been associated with depressive symptoms<sup>(28)</sup> and an increased risk of cancer<sup>(9)</sup> and all-cause mortality<sup>(29)</sup>. Habitually skipping breakfast has also been associated with higher odds of having chronic inflammation.

Recently, one cross-sectional study including 644 participants in the Cancer Prevention Study-3 Diet Assessment Sub-study assessed breakfast consumption and inflammatory status using glycoprotein acetyl as the inflammatory indicator<sup>(12)</sup>. Individuals who ate breakfast for 5 d had

higher glycoprotein acetyl ( $\beta$  0·21; 95 % CI 0·03, 0·40) when compared with those who consumed breakfast on all 6 d. However, no association was found for other exposure groups, which could be due to the small sample size of those groups<sup>(12)</sup>. Interestingly, irregularity in breakfast consumption, as assessed by the intra-individual sp of time at first intake of the day, was significant associated with high glycoprotein acetyl<sup>(12)</sup>. Consistently, in a previous cross-sectional study including 18 777 Italian adults, a breakfast score was developed based on the consumption of 'typical





Italian breakfast foods', including milk, coffee, tea, yogurt, crispbread/rusks, breakfast cereals, brioche, biscuits, honey, sugar and jam<sup>(11)</sup>. Relative to individuals in the lowest breakfast foods score quintile, those in the highest quintile had lower CRP (1.35~v.~1.57~mg/l) and lower odds of having CRP  $\geq 1.0~mg/l$  (adjusted OR 0.83,~95% CI 0.73,~0.93)<sup>(11)</sup>.

Our findings are consistent with previous studies that link breakfast behaviour and chronic disease risk. Habitually skipping breakfast has been associated with increased risk of CVD<sup>(5,11,30)</sup>, type II diabetes<sup>(3,31)</sup>, obesity<sup>(32)</sup> and cancer<sup>(7)</sup>. For example, in a study based on the National Health and Nutrition Examination Survey III, participants who did not consume breakfast had a significantly increased risk of CVD mortality, after adjustment for age, sex, race, socioeconomic status, dietary and lifestyle factors, BMI and other conventional cardiovascular risk factors<sup>(33)</sup>. Similarly, in the Health Professionals Follow-Up Study, including 26 902 men, Cahill et al. (5) found that habitual breakfast skippers had a 27 % higher risk of myocardial infarction as compared with breakfast eaters during 16 years of follow-up. A meta-analysis also reported that skipping breakfast was associated with obesity (pooled OR 1.75, 95 % CI 1.57, 1.95)(32). While the mechanisms connecting breakfast consumption and chronic disease risk are not fully understood, increased inflammation in breakfast skippers has been suggested as one potential pathway connecting the two<sup>(34)</sup>.

CVD and the aforementioned chronic conditions are associated with elevated CRP<sup>(6,8)</sup>. Hence, our findings that habitual breakfast skipping is associated with chronic inflammation (increased plasma CRP) support the hypothesis that breakfast skipping may increase inflammatory biomarkers and thus increase the risk of chronic inflammatory diseases like CVD.

Several potential mechanisms may explain the connection between skipping breakfast and chronic inflammation. First, breakfast consumption is positively related to appetite control<sup>(35)</sup>, and subsequently, appetite control affects glycaemic control. Omission of breakfast could impair glycaemic control by interfering with insulin sensitivity and increasing the likelihood of overeating later in the day. An impaired glycaemic control alters postprandial inflammatory responses. When TAG and glucose rise postprandially, neutrophil counts increase codependent with production of pro-inflammatory cytokines and oxidative stress<sup>(36,37)</sup>. Second, breakfast skipping leads to a prolonged overnight fasting period, which may be regarded as a state of stress (34,37). This stress increases adrenergic activity and elevated blood pressure that could lead to increased inflammatory responses, although contradictory data suggested that intermittent fasting with prolonged fasting time could be associated with improved metabolic parameters<sup>(38,39)</sup>. Further, habitual breakfast skippers are more likely to make unhealthy lifestyle choices such as smoking, physical inactivity and irregular meal times, compared with regular breakfast eaters<sup>(7,40)</sup>. However, in our study, the inverse association between breakfast consumption and plasma CRP concentration remained, even after adjusting for these lifestyle factors.

The association between breakfast and lower inflammatory status as assessed by CRP concentrations appeared to be stronger among older adults and those who had poor overall diet quality. Ageing and poor diet quality are well-documented risk factors for chronic inflammation and CVD<sup>(41-43)</sup>. In the subgroup analysis, stratified by diet quality score, we observed a significant association between breakfast skipping and elevated CRP concentration among individuals with low diet score. This is expectable because poor diet is generally associated with low consumption of anti-inflammatory foods, such as fruit, vegetables and whole grain<sup>(43)</sup>. Skipping breakfast, together with poor diet quality, may lead to synergistic effects that aggravate inflammatory state (34,37). Although the underlying mechanisms remain unclear, our findings suggest the importance of breakfast consumption in these vulnerable populations. In contrast, insignificant breakfast-CRP relationship was observed among those with high diet quality. This suggests that in individuals with higher diet quality, their lower CRP concentrations compared with breakfast skippers could be attributed largely to the healthier overall diet quality, relative to modest impact of breakfast behaviour.

The 'breakfast 1–2 times/week' group appeared to not fit with the overall CRP concentration trends. However, this should be interpreted with caution because the sample size is smaller in this group, relative to other breakfast consumption groups. Thus, this could be due to chance. Another potential explanation is that this group has the youngest age (mean age  $41.7\ v.\ 44.4$ –53 years in other groups) among all breakfast frequency groups. As mentioned previously, ageing is a major determinant of chronic inflammation status<sup>(41,44)</sup>.

Our study has several strengths, including the large sample size and adjustment for a wide range of potential confounders, such as overall diet quality and total energy. Moreover, unlike previous studies on this topic, we also adjusted for several sleep parameters, such as sleep duration, snoring and insomnia in our models because these conditions have been shown to be associated with altered CVD risk and could be relevant to breakfast consumption behaviour(45-47). There are also several limitations in the current study. Women (17.7 % of all participants) are under-represented. However, the sample size of women (n 12 458) remains sufficiently large to explore whether the breakfast-inflammation relation could be modified by sex. We used selfreport questionnaires to assess breakfast consumption frequency, which could introduce misclassification. Further, previous studies reported that different breakfast foods and breakfast food patterns might have different impacts on cardiometabolic risk<sup>(48,49)</sup>. However, we





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did not collect information on the specific foods which were consumed during breakfast.

#### **Conclusions**

In this large cohort of Chinese adults, we found that habitually skipping breakfast is associated with chronic inflammation, as assessed by CRP concentration, among individuals without CVD, suggesting that the previously observed association between breakfast consumption and altered chronic disease risk could be partially mediated through the effect of regular breakfast consumption on chronic inflammation. These findings should be replicated in future prospective studies with repeated assessment of inflammatory biomarkers (e.g., CRP and IL 6). Future studies should also include detailed information on type and amount of breakfast foods consumed.

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# Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S1368980020001214

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