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A Prospective Study of Breakfast Eating and Incident Coronary Heart Disease in a Cohort of Male U.S. Health Professionals

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Abstract

Background—Among adults, skipping meals is associated with excess bodyweight, hypertension, insulin resistance, and elevated fasting lipid concentrations. However, it remains unknown whether specific eating habits irrespective of dietary composition influence coronary heart disease (CHD) risk. The objective of this study was to prospectively examine eating habits and risk of CHD.

Methods and Results—Eating habits including breakfast eating were assessed in 1992 in 26,902 American men aged 45-82 years from the Health Professionals Follow-up Study who were free of cardiovascular disease and cancer. During 16 years of follow-up, 1,527 incident CHD cases were diagnosed. Cox proportional hazards models were used to estimate relative risks (RR) and 95% confidence intervals (CI) for CHD, adjusted for demographic, diet, lifestyle, and other CHD risk factors. Men who skipped breakfast had a 27% higher risk of CHD as compared with men who did not (RR=1.27, 95% CI:1.06-1.53). Compared with men who did not eat late at night, those who ate late at night had a 55% higher CHD risk (RR=1.55, 95% CI:1.05-2.29). These associations were mediated by BMI, hypertension, hypercholesterolemia and diabetes. No association was observed between eating frequency (times/day) and risk of CHD.

Conclusions—Eating breakfast was associated with significantly lower CHD risk in this cohort of male health professionals.

Keywords

coronary disease; epidemiology; myocardial infarction; nutrition; prevention

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INTRODUCTION

Although it is commonly stated that breakfast is the most important meal of the day, there exist no evidence-based recommendations for adults regarding eating habits (the frequency and or timing of meals, snacks, and caloric beverages). The 2010 Dietary Guidelines for Americans recommend breakfast for children, but make no recommendation for adults, stating "behaviors have been studied, such as snacking and frequency of eating, but there is currently not enough evidence to support a specific recommendation for these behaviors".[1]

Results from the 2002 NHANES survey suggest that snacking and skipping breakfast are common practices among American adults, with 18% skipping breakfast and 86% snacking each day.[2] The Nationwide Food Consumption Survey 1965-1991 reported that breakfast consumption is down from 86% (1965) to 75% (1991).[3] This trend may have adverse consequences at a population level because results from short-duration trials, preliminary cross-sectional studies and small prospective studies report that eating habits such as skipping meals have been positively associated with several cardio-metabolic health outcomes including overweight[4] and weight gain,[5] dyslipidemia,[6, 7] blood pressure[8], insulin sensitivity[6, 7] and diabetes.[9] However, to our knowledge, no human studies of eating habits and coronary heart disease (CHD) have been published. The objective of our study was to prospectively determine whether eating habits, including skipping breakfast, are related to increased risk of CHD.

METHODS

Study Population

The Health Professionals Follow-up Study (HPFS) is an ongoing prospective study of 51,529 male health professionals (dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists) aged 40-75 years at enrolment in 1986. Approximately 97% of participants were of white European descent. Participants have been followed through mailed biennial questionnaires which ascertained medical history, lifestyle, and health-related behaviors, as previously described.[10, 11] This study was approved by the Institutional Review Board of the Harvard School of Public Health, Boston, Massachusetts, and all participants gave informed consent. Baseline for the present analysis was in 1992 when eating habits were first assessed. The follow-up period for each participant started at the month of return of the 1992 questionnaire through confirmed CHD outcome, death or January 31st 2008. Men were excluded from the analysis if they died between 1986 and 1992 (n=1,758) or did not complete the FFQ dietary assessment (n=14,776; includes men who dropped out before 1992, men who received a shorter version of the questionnaire without questions on diet because they not respond to the full questionnaire after four mailings, and men who reported total energy intake outside of 800-4200 calories/day). By 1992, the 0.5% who were lost to follow-up were on average 7 years older, 12% more smoked, 7% more had hypertension, 4% more had diabetes and 7% less ate breakfast as compared to the participants who were not lost to follow-up. Men were excluded from the present analysis if they did not answer the eating habits question (n=2,123), had cancer (except non-melanoma skin cancer) or a history of cancer (n=2,041), CHD or a history of MI (n=1,528), angina or a history of angina (n=1,601) and stroke or a history of stroke (n=800). After exclusions, the final sample size was 26,902 men. The characteristics of participant in our sample were not substantially different from those of the original full cohort at baseline.[12, 13]

Eating Habits and other Dietary Assessment

In 1992, HPFS participants were asked to respond to the following question: 'Please indicate the times of day that you usually eat (*mark all that apply*): before breakfast, breakfast, between breakfast and lunch, lunch, between lunch and dinner, dinner, between dinner and bed time, and after going to bed'. We totaled the number of responses to calculate a participant's eating frequency per day. Because some men who reported skipping breakfast also reported that they ate before breakfast (3%) or between breakfast and lunch (20%), we defined breakfast as a positive response to any of the first three eating times ('before breakfast', 'breakfast', 'between breakfast and lunch') in order to differentiate those who broke fast from those who did not break fast. We defined late night eating as a positive response to 'after going to bed'.

In the HPFS, diet over the previous year is assessed every 4 years using a 131-item food frequency questionnaire (FFQ). Nutrient intakes were calculated by converting the frequency responses to daily intakes for each food or beverage, multiplying the daily intakes of each food and beverage with its corresponding nutrient content, and summing the contributions of all items. The validity and reproducibility of the FFQ have been reported elsewhere.[14, 15] To assess the overall diet quality of the participants, a diet score for each participant was calculated[16] based on the 2010 Alternate Healthy Eating Index (AHEI) which was designed to target food choices and macronutrient sources that have been associated with reduced chronic disease risk.

Assessment of CHD Outcomes and Intermediates

Incident CHD was defined as non-fatal myocardial infarction (MI) or fatal CHD. On each biennial questionnaire, participants were asked whether they had experienced an MI, and when an event was reported, it was confirmed by review of medical records and autopsy reports by study physicians blinded to participant's exposure status. MI was diagnosed using the World Health Organization's criteria (symptoms plus either diagnostic electrocardiographic changes or elevated levels of cardiac enzymes).[17] Fatal CHD was confirmed by hospital records or an autopsy. Between return of the 1992 questionnaire and January 31st 2008, there were 1,527 incident CHD cases.

On each biennial questionnaire, participants were asked for their weight and whether they had been 'professionally-diagnosed' with any of a long list of health conditions including diabetes, hypercholesterolemia and hypertension. BMI (kg/m^2) was calculated using the self-reported weight and most recently reported height. Weights reported on the questionnaires were validated in a subsample of 123 men from the HPFS in which self-reported and measured weights were found to be highly correlated (Pearson correlation of 0.97).[18] Similarly, the validity of the self-reported diabetes has been documented previously in the HPFS with confirmation by supplementary questionnaire and medical records.[19] Diabetes was defined according to the National Diabetes Data Group criteria[20] until 1997 when the fasting plasma glucose threshold for the diagnosis diabetes was changed to the American Diabetes Association criteria.[21] Validation against medical records has also shown that hypertension is accurately self-reported by HPFS participants,[22] and although the soundness of self-reported hypercholesterolemia has not been assessed in the HPFS, it has been successfully validated in a cohort of nurses using the same biennial questionnaire.[23]

Statistical Analysis

To examine associations between eating habits and CHD, we used Cox proportional hazards models stratified on age (in months) and follow-up cycle to estimate relative risks (RR) and 95% confidence intervals (CI). In addition to breakfast and late night eating, we also evaluated the other individual meals and snacks as well as eating frequency (total eating

times/day) in relation to risk of CHD. We further coded the eating habits data into new variables that categorized participants by their breakfast eating status combined with eating frequency, or by their number of eating occasions (snacks) in addition to the 3 main meals (breakfast, lunch, and dinner), and analyzed these variables in relation to CHD risk.

Multivariate models were adjusted for known and suspected risk factors of CHD such as energy intake (quintiles of kilocalories/day), alcohol intake (0, 0.1-<5, 5-<15, 15-<30, 30+ g/day), diet quality using the 2010 AHEI (quintiles of score), physical activity (quintiles of MET-hours/week), television watching (asked in categories 0-1.5, 2.0-6.0, 7.0-20.0, ≥21.0 hours/week), sleep (<7, 7-8, >8 hours/24 hours), smoking status (never, past, current), marital status (married, not married), full-time work status (yes, no), had a physical exam in last two years (yes, no) and family history of CHD before the age of 60 (yes, no). We then additionally adjusted for potential mediators, including diabetes (yes, no), hypertension (yes, no), hypercholesterolemia (yes, no), and BMI (<18.5,18.5-24.9, 25-29.9, 30+ kg/m^2). These variables were updated for each 2-year follow-up period, as were all covariates with the exception of dietary covariates, which were updated every 4 years. Cumulative averages of dietary covariates were calculated at each time point to better represent long-term diet and to minimize within-person variation.[24] Dietary covariates were not updated if there was a diagnosis of intermediates of CHD including diabetes, hypertension and hypercholesterolemia, as individuals with these conditions may change their diet.[25] Although less than 2% of data were missing for any variable, indicator variables with a separate level for missing were created. Complete case analysis and multiple imputation analysis (10 imputations) were also conducted to compare results from different methods of approaching missing data. Proportional hazards assumptions were not violated for any of the covariates. In models where eating frequency was not the main exposure, we adjusted for the number of eating times (continuous). In sensitivity analyses, we further adjusted for aspirin use (yes, no), antidepressant medication (yes, no), daily number of cigarettes among smokers (1-14, 15-24, 25+ cigarettes/day), reported stress in the workplace or at home (yes, no), bodyweight gain (continuous), and quintiles of specific nutrients such as dietary folate, whole grains, fiber, and saturated fat, all residually adjusted for energy. A sensitivity analysis employing models with the original continuous versions of continuously-gathered covariates was conducted for comparison to categorical use of these originally-continuous variables. To evaluate if the association between late night eating and risk of CHD was due to underlying sleep apnea, known to be more common in late night eaters,[26, 27] we conducted a sensitivity analysis excluding participants with BMI ≥ 30 kg/m^2 and another sensitivity analysis excluding participants who snore, as proxies for sleep apnea. We used these proxies because the most significant risk factor for sleep apnea is obesity,[28] while habitual snoring is the most common symptom of sleep apnea, reported in 70-95% of individuals with sleep apnea.[28] We conducted stratified analyses for each known CHD risk factor to determine if any interactions existed between any of the risk factors and an eating habit (breakfast, late night eating, eating frequency) on risk of CHD. SAS version 9.2 (SAS, Cary, NC, USA) was used for all analyses.

RESULTS

Participants who did not report eating breakfast were younger than those who did, and were more likely to be smokers, employed full time, unmarried, less physically active, and drink more alcohol (Table 1). Men who ate breakfast ate on average one more time per day than those who skipped breakfast, implying that those who abstained from breakfast were not eating additional make-up meals later in the day. Although there was some overlap between those who skipped breakfast and those who ate late at night, 76% of late night eaters ate breakfast (data not shown). Men who reported that they ate late at night were more likely to smoke, sleep less than seven hours a night, or have baseline hypertension as compared to

men who did not eat late at night. The late night eating abstainers were more likely to be married and work full time and ate on average one time less per day that the late night eaters. The mean diet quality of the participants, as measured by the AHEI, was very high among HPFS participants, regardless of their breakfast or late night eating status.

In age-adjusted models, men who did not eat breakfast had a 33% higher risk of CHD as compared with men who did (RR=1.33, 95% CI: 1.13-1.57) (Table 2). This risk was similar (RR=1.27, 95% CI: 1.06-1.53) when also adjusted for diet, demographic and activity factors, but was attenuated (RR=1.18, 95% CI: 0.98-1.43) when further adjusted for the potential mediators of BMI, hypercholesterolemia, hypertension and diabetes. A sensitivity analysis employing models with the original continuous versions of continuously-gathered covariates yielded similar results as to when these variables were categorized in models (data not shown). Compared with men who did not eat late at night, those who ate late at night had a 55% higher risk of CHD (multivariate RR=1.55, 95% CI: 1.05-2.29) (Table 3). When we conducted the same analysis removing all participants with a BMI ≥ 30 kg/m^2, the association was not appreciably different (multivariate RR=1.58, 95% CI: 1.02-2.46; analysis contained 1,318 incident CHD events) (data not shown). When we conducted the analysis removing all participants who snore, the association was modestly stronger (multivariate RR=1.97, 95% CI: 1.21-3.20; analysis contained 823 incident CHD events) (data not shown). When we further adjusted for potential mediators of diabetes, hypertension and hypercholesterolemia, the association between late night eating and CHD risk was attenuated (RR=1.41, 95% CI: 0.95-2.08).

No association was observed between eating frequency and risk of CHD (Table 4). For example, compared to men who ate 3 times/day, men who ate 1-2 times/day had a multivariate RR (95% CI) of 1.10 (0.92-1.32), while men who ate 4-5 times/day and 6+ times/day had RRs of 1.05 (0.94-1.18) and 1.26 (0.90-1.77) respectively. We also did not observe a new pattern of association between risk of CHD and eating habits using the variables we created that combined eating frequency with breakfast eating or examined snacking outside of the 3 main meals (data not shown). Results for the breakfast and late night eating analyses were not materially altered by further adjustment for each other, stress, aspirin use, antidepressant medication, daily number of cigarettes among smokers, bodyweight change every four years and specific dietary components such as folate, whole grains, fiber or saturated fat. Exclusion of participants with diabetes, hypertension or hypercholesterolemia at baseline also did not materially alter results even though the number of participants was reduced to 13,729 men with 532 CHD events. For example, compared to men who ate breakfast, men who skipped breakfast had an RR (95% CI) of CHD of 1.48 (1.12-1.94) in models adjusted for only age, an RR (95% CI) of 1.40 (1.03-1.91) when further adjusted for diet, demographic and activity factors, and an attenuated RR (95% CI) of 1.34 (0.98-1.83) when additionally adjusted for the development of diabetes, hypertension and hypercholesterolemia during follow-up. Results were unchanged when complete case analysis and multiple imputation were employed in place of the missing indicator approach to missing data reported (Table 5). In a sensitivity analysis that included participants who did not report eating habits, compared to participants who reported eating breakfast, those who did not answer the eating habits question had a RR (95%CI) of CHD of 1.02 (0.82-1.25). In stratified analyses, among men ≤ 60 years old, those who skipped breakfast had a 50% higher risk of CHD as compared with men who ate breakfast (multivariate RR = 1.55, 95% CI: 1.09-2.22), while this association was not significant in the older half of participants (RR = 1.06, 95%CI: 0.84-1.33, p, interaction = 0.01) (Supplementary Table 1).

DISCUSSION

In this first large prospective analysis of eating habits and CHD, we found an increased risk of CHD among men who skipped breakfast and also among men who regularly ate late at night. These associations included extensive adjustment for demographic, diet and lifestyle factors, and were mediated by BMI and the health conditions of hypertension, hypercholesterolemia and diabetes. We did not detect an association between eating frequency and risk of CHD. To the best of our knowledge, this is the first prospective analysis of eating habits and risk of CHD. However, eating habits have been shown to be associated with several CHD risk factors such as risk of overweight,[4] dyslipidemia,[6, 7] blood pressure,[8] and insulin sensitivity,[6, 7] and eating habits have also been associated with incidence of diabetes[9] and total mortality.[29] It has been previously reported in the HPFS that compared to men who ate breakfast, participants who skipped breakfast were 15% more likely to have substantial weight gain (≥5kg) during 10 years of follow-up[5] and were 21% more likely to develop type 2 diabetes.[9] Omitting breakfast has been reported to impair serum lipids and postprandial insulin sensitivity in multiple randomized crossover trials.[6, 30] A review of eight randomized controlled crossover trials examining the impact of eating habits without calorie restriction on CHD risk factors concluded that feasting (consuming all energy needs in one meal/day) was associated with higher LDL, apolipoprotein B, triglyceride and blood pressure, as compared to nibbling (eating 3+ times/day).[31] Eating frequency (times/day) in the HPFS has been previously reported to be associated with weight gain[5] and type 2 diabetes;[9] however, in the present analysis we observed no association between frequency of eating and risk of CHD.

The timing of the meal may be directly responsible for the metabolic effects that may lead to CHD, or alternatively eating habits may be a proxy for specific foods more likely to be consumed at breakfast or late at night such as breakfast cereals high in dietary fiber and fortified micronutrients like folate,[32] or late night snack foods high in calories.[33, 34] Eating habits could also be a behaviour marker for several other lifestyle characteristics that may be related to CHD, such as watching TV,[35] physical activity[36] or sleep.[37] Although modestly attenuated, our findings for both breakfast and late night eating remained significant after adjustment for multiple lifestyle-related factors and were not altered when specific nutrients such as folate and fiber were added to the model. The association between late night eating and risk of CHD was not different when we excluded participants who snore or have a BMI >30 kg/m^2, so it is unlikely that the association we observed is due either to sleep apnea or to the night-eating syndrome, which is a form of disordered eating in which the majority of an individual's food is consumed during the night, and the individual is usually obese.[38] We observed that the relationships between risk of CHD and both breakfast and late night eating were attenuated by further adjustment for the potential mediators of hypertension, diabetes, BMI and hypercholesterolemia, suggesting that eating habits may impact risk of CHD through pathways associated with these traditional risk factors. However, we were under powered with cases for a detailed mediation analysis, especially for late night eating. The late night eaters in our study represented only a small percentage of the HPFS population, and too few other population studies have reported the frequency of late night eating for an accurate assessment of whether late night eating is a common habit. Therefore, it remains unknown whether the association that we observed between late night eating and risk of CHD is relevant as a public health concern. Previously, others have reported higher rates of CHD among night shift workers[39, 40] potentially explained by disturbed circadian rhythms[41] which have been proven to influence cardiovascular health measures such as blood pressure and vascular function.[42] Thus, waking in the middle of the night to eat may increase CHD risk through these mechanisms, regardless of food intake.[43] Alternatively, altered circadian and diurnal rhythms have been shown to influence food intake[44] and have been postulated to modify the satiety and metabolism of food throughout the day. In 867 free-living men and

women, morning eating was reported as particularly satiating, while late night eating lacked satiating value and resulted in greater overall energy intake.[34] The popular belief that eating earlier in the day allows the body the rest of the day to metabolize calories and is thus weight-control protective in the same way that eating later in the day leads to weight gain has garnered scientific evidence of both opposition[45] and support[46] in human studies. Nocturnal mice fed only during a 12-hour light phase, a time when they are typically less active, gain significantly more weight than the same nocturnal mice fed only during a 12-hour dark phase.[47] A similar trial conducted in women reported that misalignment between sleep time and endogenous circadian rhythms (sleeping and eating 12 hours out of phase) produced alterations in cardio-metabolic functions such as blood pressure, heart rate and cardiac vagal modulation after controlling for sleep efficiency.[48] The influences of circadian rhythms, light/dark exposure and time-of-day eating on the metabolism of food and subsequent risk of CHD in humans require further investigation.

We did not have measurement of circadian rhythms or light/dark exposure in our study, and the HPFS participants are not physicians, nurses or other professions that regularly work night shifts, so we were unable to examine how shift work influences eating habits. The present study only had data on regular eating habits, and so we could not estimate the risk of CHD associated with occasional eating habits such as skipping breakfast a couple of days a week. However, our study had several strengths including comprehensive repeated assessment of many lifestyle characteristics gathered prospectively with a long duration of follow-up. As such, we were able to assess the modification of the association for breakfast and late night eating by other dietary components. Although we adjusted for factors such as diet quality, stress and having regular physical exams to control for a chaotic versus stable lifestyle, it is possible that eating habits could be a marker of lifestyle consistency or general health-seeking behavior. We acknowledge that the interpretation of eating habits is subjective and may have been interpreted differently by participants, especially regarding beverages such as sugar-sweetened beverages or alcoholic drinks as these may have not been included in the eating frequency assessment when consumed without food. The eating habits question was only asked once, and did not include details on the exact times of day a participant eats, or on specific nutrient composition of the different meals and snacks. Even though we did have repeated dietary assessment over the follow-up period, we cannot exclude the possibility of unmeasured confounding. The relatively homogenous study population should reduce residual confounding due to unmeasured socio-economic variability. The overall average diet quality of our study population was good, so it is not known if our results are generalizable to other populations with lower diet quality. Future studies to confirm our findings are necessary as are studies of other cardiovascular outcomes such as hypertension and stroke that may have modestly different etiologic pathways.

In conclusion, we observed in this large prospective study of middle aged and older US male health professionals that breakfast eating was associated with lowered risk of CHD. Our study was the first to assess eating habits in relation to CHD, and the associations we report are significant but modest, requiring replication. If replicated in women and other ethno-cultural groups, the findings from the present study provide evidence to support a recommendation of daily breakfast eating by clinicians and health authorities to prevent CHD and improve health at both the individual and population level.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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CLINICAL PERSPECTIVE

Among adults, skipping meals is associated with many cardio-metabolic risk factors including excess bodyweight, hypertension, insulin resistance, and elevated fasting lipid concentrations. However, there exist no formal evidence-based dietary guidelines for adults regarding eating habits such as breakfast eating, and it has remained unknown whether specific eating habits irrespective of dietary composition influence risk of major cardiovascular health outcomes such as coronary heart disease (CHD). In this first large prospective analysis of eating habits and CHD (defined as non-fatal myocardial infarction or fatal CHD), we studied a well-characterized cohort of 26,902 male American dentists, veterinarians, pharmacists, optometrists, osteopaths, and podiatrists for 16 years, taking into account comprehensive adjustment for demographic, diet and lifestyle factors. We found that men who skipped breakfast had an increased risk of CHD compared to men who ate breakfast, an association that was potentially due to a combination of the mechanistic pathways of obesity, hypertension, hypercholesterolemia and diabetes. We did not detect an association between eating frequency (the number of meals and snacks per day) and risk of CHD. Our study provides novel evidence of the benefit of breakfast consumption for the prevention of coronary events, and to our best knowledge, is the first study to investigate this topic. If confirmed in future studies of different populations, our findings support a recommendation of daily breakfast eating by clinicians and health authorities to prevent CHD and improve health at both the individual and population level.

Table 1

Baseline characteristics by both breakfast eating and late night eating status (Health Professionals Follow-up Study 1992-2008).

	Breakfast		Late Night Eating	
	Yes (n=23,516)	No (n=3,386)	No (n=26,589)	Yes (n=313)
Age*, years	59.2 (9.4)	54.1 (7.2)	58.6 (9.3)	57.9 (9.1)
Current smoker, %	5	15	7	11
Married, %	91	86	90	86
Stress at home or work, %	78	77	78	80
Work full-time, %	71	76	72	68
Physical Activity, MET-hours/week	37.7 (41.5)	33.9 (40.8)	37.1 (41.3)	38.5 (46.2)
Television ≤1.5 hours/week, %	9	7	9	7
Television ≥21 hours/week, %	10	13	10	14
Sleep <7 hours/24 hours, %	16	19	16	22
Sleep >8 hours/24 hours, %	3	5	3	6
BMI, kg/m^2	25.6 (3.3)	26.3 (3.5)	25.7 (3.3)	26.5 (4.1)
No physical exam in past 2 years, %	20	25	21	19
Parental MI <60 years of age, %	12	12	12	13
Hypercholesterolemia, %	33	36	34	39
Hypertension, %	25	28	26	37
Diabetes, %	4	2	4	5
Medication for depression, %	1	2	1	3
Aspirin use, %	32	28	31	39
Alcohol, grams/day	9.8 (13.7)	13.5 (17.9)	10.3 (14.3)	11.5 (18.1)
Drink alcohol, %	75	78	76	71
Calories, kcal/day	1954 (591)	1831 (597)	1934 (591)	2090 (690)
AHEI 2010 diet quality score	53.9 (11.6)	50.5 (11.3)	53.5 (11.6)	53.4 (11.8)
Eat 'pre-breakfast'†, %	1	0	1	4
Eat 'breakfast'†, %	96	0	84	70
Eat 'between breakfast and lunch'†, %	11	0	9	15
Late night eat, %	1	2	0	100
Eating frequency (times/day)	3.6 (0.8)	2.4 (0.7)	3.4 (0.8)	4.3 (1.2)

Values are means (SD) or percentages and are standardized to the age distribution of the study population. AHEI is alternate healthy eating index; BMI is body mass index; MET is metabolic equivalent; MI is myocardial infarction.

*Value is not age adjusted.

†Exact wording of eating habits question on questionnaire. We defined breakfast as a positive response to any of these three eating times ('before breakfast', 'breakfast', 'between breakfast and lunch') in order to differentiate those who broke fast from those who did not break fast.

Table 2

Eating breakfast and multivariate relative risk (RR) of coronary heart disease (CHD) with 95% confidence intervals (CI).

	Breakfast		
	Yes	**No**	**p-value**
N cases	1356	171	
Person Years	338,074	49,880	
Age adjusted model: RR (95% CI)	1.00 (Ref)	1.33 (1.13, 1.57)	0.0008
+ Diet factors *	1.00 (Ref)	1.38 (1.15, 1.66)	0.0006
+ Demographic factors †	1.00 (Ref)	1.29 (1.07, 1.55)	0.007
+ Activity factors ‡	**1.00 (Ref)**	**1.27 (1.06, 1.53)**	**0.01**
Adjustment for Potential Mediators			
+ BMI §	1.00 (Ref)	1.23 (1.02, 1.48)	0.03
+ Health conditions /	1.00 (Ref)	1.21 (1.00, 1.46)	0.05
+ BMI & health conditions	**1.00 (Ref)**	**1.18 (0.98, 1.43)**	**0.08**

* Diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/day), alcohol intake (0, 0.1-<5, 5-<15, 15-<30, 30+ g/day, missing), eating frequency (1-8 times/day).

† Demographic factors: smoking (never, past, current), marital status (yes, no, missing), full-time work status (yes, no, missing), parental myocardial infarction <60 years of age (yes/no), physical exam in last two years (yes/no).

‡ Activity factors: physical activity (quintiles MET hours/week), television (asked in categories 0-1.5, 2.0-6.0, 7.0-20.0, ≥21.0 hours/week, missing), sleep (<7, 7-8, >9 hours/24 hours, missing).

§ In addition to diet, demographic and activity factors, this model is further adjusted for BMI updated every 2 years (<18.5, 18.5-24.9, 25-29.9, 30+ kg/m^2, missing).

/ In addition to diet, demographic and activity factors, this model is further adjusted for diabetes (yes/no), hypertension (yes/no) and hypercholesterolemia (yes/no), updated every 2 years.

Further adjustment for late night eating, stress, antidepressant medication, daily number of cigarettes among smokers, bodyweight change and specific dietary components such as folate, whole grains, fiber or saturated fat did not substantially alter results.

Table 3

Late night eating and multivariate relative risk (RR) of coronary heart disease (CHD) with 95% confidence intervals (CI).

	Late Night Eat		
	No	**Yes**	**p-value**
N cases	1498	29	
Person years	383,584	4370	
Age adjusted model: RR (95% CI)	1.00 (Ref)	1.61 (1.10, 2.36)	0.01
+ Diet factors *	1.00 (Ref)	1.59 (1.08, 2.35)	0.02
+ Demographic factors †	1.00 (Ref)	1.55 (1.05, 2.28)	0.03
+ Activity factors ‡	**1.00 (Ref)**	**1.55 (1.05, 2.29)**	**0.03**
Adjustment for Potential Mediators			
+ BMI §	1.00 (Ref)	1.53 (1.04, 2.25)	0.03
+ Health conditions /	1.00 (Ref)	1.41 (0.95, 2.10)	0.08
+ BMI & health conditions	**1.00 (Ref)**	**1.41 (0.95, 2.08)**	**0.09**

* Diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/day), alcohol intake (0, 0.1-<5, 5-<15, 15-<30, 30+ g/day, missing), eating frequency (1-8 times/day).

† Demographic factors: smoking (never, past, current), marital status (yes, no, missing), full-time work status (yes, no, missing), parental myocardial infarction <60 years of age (yes/no), physical exam in last two years (yes/no).

‡ Activity factors: physical activity (quintiles MET hours/week), television (asked in categories 0-1.5, 2.0-6.0, 7.0-20.0, ≥21.0 hours/week, missing), sleep (<7, 7-8, >9 hours/24 hours, missing).

§ In addition to diet, demographic and activity factors, this model is further adjusted for BMI updated every 2 years (<18.5, 18.5-24.9, 25-29.9, 30+ kg/m^2, missing).

/ In addition to diet, demographic and activity factors, this model is further adjusted for diabetes (yes/no), hypertension (yes/no) and hypercholesterolemia (yes/no), updated every 2 years.

Further adjustment for breakfast, stress, antidepressant medication, daily number of cigarettes among smokers, bodyweight change and specific dietary components such as folate, whole grains, fiber or saturated fat did not substantially alter results.

Table 4

Eating frequency and multivariate relative risk (RR) of coronary heart disease (CHD) with 95% confidence intervals (CI).

	1-2 times/day	3 times/day	4-5 times/day	6+ times/day
N cases	150	728	611	38
Person years	39,868	183,947	155,731	8,408
Age adjusted RR (95% CI)	1.17 (0.97, 1.40)	1.00 (Ref)	1.08 (0.97, 1.20)	1.30 (0.93, 1.82)
+ Diet factors*	1.13 (0.95, 1.36)	1.00 (Ref)	1.06 (0.95, 1.19)	1.26 (0.90, 1.77)
+ Demographic factors†	1.10 (0.92, 1.32)	1.00 (Ref)	1.06 (0.95, 1.19)	1.28 (0.91, 1.79)
+ Activity factors‡	**1.10 (0.92, 1.32)**	**1.00 (Ref)**	**1.05 (0.94, 1.18)**	**1.26 (0.90, 1.77)**
Adjustment for Potential Mediators				
+ BMI§	1.09 (0.91, 1.31)	1.00 (Ref)	1.03 (0.92, 1.15)	1.25 (0.89, 1.75)
+ Health conditions‖	1.08 (0.90, 1.30)	1.00 (Ref)	1.01 (0.90, 1.13)	1.15 (0.82, 1.61)
+ BMI & health conditions	**1.08 (0.90, 1.29)**	**1.00 (Ref)**	**1.00 (0.89, 1.11)**	**1.14 (0.81, 1.61)**

*Diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/day), alcohol intake (0, 0.1-<5, 5-<15, 15-<30, 30+ g/day, missing).

†Demographic factors: smoking (never, past, current), marital status (yes, no, missing), full-time work status (yes, no, missing), parental myocardial infarction <60 years of age (yes/no), physical exam in last two years (yes/no).

‡Activity factors: physical activity (quintiles MET hours/week), television (asked in categories 0-1.5, 2.0-6.0, 7.0-20.0, ≥21.0 hours/week, missing), sleep (<7, 7-8, >9 hours/24 hours, missing).

§In addition to diet, demographic and activity factors, this model is further adjusted for BMI updated every 2 years (<18.5, 18.5-24.9, 25-29.9, 30+ kg/m^2, missing).

‖In addition to diet, demographic and activity factors, this model is further adjusted for diabetes (yes/no), hypertension (yes/no) and hypercholesterolemia (yes/no), updated every 2 years.

Further adjustment for breakfast, late night eating, stress, antidepressant medication, daily number of cigarettes among smokers, bodyweight change and specific dietary components such as folate, whole grains, fiber or saturated fat did not substantially alter results.

Table 5

Comparison of eating habits and multivariate relative risk (RR) of coronary heart disease (CHD) with 95% confidence intervals (CI) obtained using different methods for approaching missing covariate data.

	Method for Missing Covariate Data		
	Missing Indicator	Multiple Imputation	Complete Case*
Risk Factor	**RR (95% CI)**	**RR (95% CI)**	**RR (95% CI)**
Skipping breakfast†	1.27 (1.06-1.53)	1.29 (1.07-1.56)	1.25 (1.03-1.51)
Late night eating‡	1.55 (1.05-2.29)	1.53 (1.01-2.32)	1.52 (1.01-2.29)
Eating frequency			
1-2 times/day	1.10 (0.91-1.31)	1.17 (0.86-1.58)	1.08 (0.79-1.47)
3 times/day	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
4-5 times/day	1.05 (0.94-1.18)	1.05 (0.79-1.38)	1.11 (0.84-1.47)
6+ times/day	1.26 (0.90-1.77)	1.21 (0.56-2.61)	1.57 (0.72-3.42)

*There are 97 fewer cases.

†The reference group is breakfast eaters.

‡The reference group is those who do not eat late at night.

The model is adjusted for age, diet quality (alternate Healthy Eating Index 2010 score), energy intake, alcohol intake, smoking, marital status, full-time work status, parental myocardial infarction <60 years of age, physical exam in last two years, physical activity (MET hours/week), television hours/week, and sleep hours/24 hours.