Prospective Study of Breakfast Eating and Incident Coronary Heart Disease in a Cohort of Male US Health Professionals

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Background—Among adults, skipping meals is associated with excess body weight, hypertension, insulin resistance, and elevated fasting lipid concentrations. However, it remains unknown whether specific eating habits regardless 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 45 to 82 years of age from the Health Professionals Follow-up Study who were free of cardiovascular disease and cancer. During 16 years of follow-up, 1527 incident CHD cases were diagnosed. Cox proportional hazards models were used to estimate relative risks and 95% confidence intervals for CHD, adjusted for demographic, diet, lifestyle, and other CHD risk factors. Men who skipped breakfast had a 27% higher risk of CHD compared with men who did not (relative risk, 1.27; 95% confidence interval, 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 (relative risk, 1.55; 95% confidence interval, 1.05–2.29). These associations were mediated by body mass index, hypertension, hypercholesterolemia, and diabetes mellitus. No association was observed between eating frequency (times per day) and risk of CHD.

Conclusions—Eating breakfast was associated with significantly lower CHD risk in this cohort of male health professionals. **(*Circulation*. 2013;128:337–343.)**

Key Words: coronary disease ■ epidemiology ■ myocardial infarction ■ nutritional sciences ■ prevention & control

Although it is commonly stated that breakfast is the most important meal of the day, no evidence-based recommendations exist for adults in terms of 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]

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Results from the 2002 National Health and Nutrition Examination Survey (NHANES) 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 to 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 cardiometabolic health outcomes, including overweight[4] and weight gain,[5] dyslipidemia,[6,7] blood pressure,[8] insulin sensitivity,[6,7] and diabetes mellitus.[9] However, to the best of 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 an 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) 40 to 75 years of age at enrollment in 1986. Approximately 97% of

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participants were of white European descent. Participants have been followed up through mailed biennial questionnaires that 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, MA, 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 31, 2008. Men were excluded from the analysis if they died between 1986 and 1992 (n=1758) or did not complete the food frequency questionnaire 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 4 mailings, and men who reported total energy intake outside 800–4200 cal/d). 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 mellitus, and 7% fewer ate breakfast compared with 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=2123) or had cancer (except nonmelanoma skin cancer) or a history of cancer (n=2041), CHD or a history of myocardial infarction (n=1528), angina or a history of angina (n=1601), and stroke or a history of stroke (n=800). After exclusions, the final sample size was 26 902 men. The characteristics of the participants 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 prompt: "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 3 eating times (before breakfast, breakfast, between breakfast and lunch) to differentiate those who broke fast from those who did not break fast. We defined late-night eating as a positive response to eating after going to bed.

In the HPFS, diet over the previous year is assessed every 4 years with a 131-item food frequency questionnaire. Nutrient intakes were calculated by converting the frequency of 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 food frequency questionnaire have been reported elsewhere.[14,15] To assess the overall diet quality of the participants, a diet score for each participant was calculated[16] on the basis of the 2010 Alternate Healthy Eating Index, 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 nonfatal myocardial infarction or fatal CHD. On each biennial questionnaire, participants were asked whether they had experienced a myocardial infarction, and when an event was reported, it was confirmed by review of medical records and autopsy reports by study physicians blinded to the participant's exposure status. Myocardial infarction was diagnosed with the World Health Organization's criteria (symptoms plus either diagnostic ECG 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 31, 2008, there were 1527 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 mellitus, hypercholesterolemia, and hypertension. Body mass index (BMI) 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=0.97).[18] Similarly, the validity of self-reported diabetes mellitus has been documented previously in the HPFS with confirmation by supplementary questionnaire and medical records.[19] Diabetes mellitus was defined according to the National Diabetes Data Group criteria[20] until 1997 when the fasting plasma glucose threshold for the diagnosis of diabetes mellitus was changed to the American Diabetes Association criterion.[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 by age (in months) and follow-up cycle to estimate relative risks (RRs) and 95% confidence intervals (CIs). In addition to breakfast and late-night eating, we evaluated the other individual meals and snacks and eating frequency (total eating times per day) in relation to the 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 per day), alcohol intake (0, 0.1–<5, 5–<15, 15–<30, ≥30 g/d), diet quality using the 2010 Alternate Healthy Eating Index (quintiles of score), physical activity (quintiles of metabolic equivalent hours per week), television watching (asked in categories 0–1.5, 2.0–6.0, 7.0–20.0, ≥21.0 h/wk), sleep (<7, 7–8, >8 h/24 h), smoking status (never, past, current), marital status (married, not married), full-time work status (yes, no), a physical examination in the last 2 years (yes, no), and family history of CHD <60 years of age (yes, no). We then additionally adjusted for potential mediators, including diabetes mellitus (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 except 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 mellitus, hypertension, and hypercholesterolemia, because individuals with these conditions may change their diet.[25] Although <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 in which 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 a day), reported stress in the workplace or at home (yes, no), body weight 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 using models with the original continuous versions of continuously gathered covariates was conducted for comparison with categorical use of these originally continuous variables. To evaluate whether the association between late-night eating and risk of CHD was attributable 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] whereas habitual snoring is the most common symptom of sleep apnea, reported in

70% to 95% of individuals with sleep apnea.[28] We conducted stratified analyses for each known CHD risk factor to determine whether 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) 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, to work full time, to be unmarried, to be less physically active, and to drink more alcohol (Table 1). Men who ate breakfast ate on average 1 more time per day than those who skipped breakfast, implying that those who abstained from breakfast were not eating additional makeup 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, to sleep <7 hours a night, or to have baseline hypertension compared with men who did not eat late at night. The late-night eating abstainers were more likely to be married and to work full time and ate on average 1 time less per day that the late-night eaters. The mean diet quality of the participants, as measured by the Alternate Healthy Eating Index, 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 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 and 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 mellitus. A sensitivity analysis using models

Table 1. Baseline Characteristics by Both Breakfast Eating and Late-Night Eating Status (Health Professionals Follow-up Study, 1992 to 2008)

	Breakfast		Late-Night Eating	
	Yes (n=23 516)	No (n=3386)	No (n=26 589)	Yes (n=313)
Age, y*	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-h/wk	37.7 (41.5)	33.9 (40.8)	37.1 (41.3)	38.5 (46.2)
Television ≤1.5 h/wk, %	9	7	9	7
Television ≥21 h/wk, %	10	13	10	14
Sleep <7 h/24 h, %	16	19	16	22
Sleep >8 h/24 h, %	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 examination in past 2 y, %	20	25	21	19
Parental MI <60 y of age, %	12	12	12	13
Hypercholesterolemia, %	33	36	34	39
Hypertension, %	25	28	26	37
Diabetes mellitus, %	4	2	4	5
Medication for depression, %	1	2	1	3
Aspirin use, %	32	28	31	39
Alcohol, g/d	9.8 (13.7)	13.5 (17.9)	10.3 (14.3)	11.5 (18.1)
Drink alcohol, %	75	78	76	71
Caloric intake, kcal/d	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 "prebreakfast," %†	1	0	1	4
Eat "breakfast," %†	96	0	84	70
Eat "between breakfast and lunch," %†	11	0	9	15
Eat late-night, %	1	2	0	100
Eating frequency, times/d	3.6 (0.8)	2.4 (0.7)	3.4 (0.8)	4.3 (1.2)

AHEI indicates Alternate Healthy Eating Index; BMI, body mass index; MET, metabolic equivalent; and MI is myocardial infarction. Values are means (SD) or percentages and are standardized to the age distribution of the study population.

*Value is not age adjusted.

†Exact wording of eating habits question on questionnaire. We defined breakfast as a positive response to any of these 3 eating times (before breakfast, breakfast, between breakfast and lunch) to differentiate those who break fast from those who did not break fast.

Table 2. Eating Breakfast and Multivariate RR of CHD With 95% CIs

	Breakfast		
	Yes	No	*P* Value
Cases, n	1356	171	
Person-years	338 074	49 880	
Age-adjusted model: RR (95% CI)	1.00 (Referent)	1.33 (1.13–1.57)	0.0008
+Diet factors*	1.00 (Referent)	1.38 (1.15–1.66)	0.0006
+Demographic factors†	1.00 (Referent)	1.29 (1.07–1.55)	0.007
+Activity factors‡	1.00 (Referent)	1.27 (1.06–1.53)	0.01
Adjustment for potential mediators			
+BMI§	1.00 (Referent)	1.23 (1.02–1.48)	0.03
+Health conditions‖	1.00 (Referent)	1.21 (1.00–1.46)	0.05
+BMI and health conditions	1.00 (Referent)	1.18 (0.98–1.43)	0.08

BMI indicates body mass index; CHD, coronary heart disease; CI, confidence interval; and RR, relative risk.

*In addition to age, this model is further adjusted for diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/d), alcohol intake (0, 0.1–<5, 5–<15, 15–<30, ≥30 g/d, missing), and eating frequency (1–8 times a day).

†In addition to age and diet factors, this model is further adjusted for 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), and physical examination in last 2 years (yes/no).

‡In addition to age, diet and demographic factors, this model is further adjusted for activity factors: physical activity (quintiles of metabolic equivalent h/wk), television (asked in categories 0–1.5, 2.0–6.0, 7.0–20.0, ≥21.0 h/wk, missing), and sleep (<7, 7–8, >9 h/24 h, missing).

§In addition to age, 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 age, diet, demographic, and activity factors, this model is further adjusted for diabetes mellitus (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, body weight 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 RR of CHD With 95% CIs

	Late-Night Eating		
	No	Yes	*P* Value
Cases, n	1498	29	
Person-years	383 584	4370	
Age-adjusted model: RR (95% CI)	1.00 (Referent)	1.61 (1.10–2.36)	0.01
+Diet factors*	1.00 (Referent)	1.59 (1.08–2.35)	0.02
+Demographic factors†	1.00 (Referent)	1.55 (1.05–2.28)	0.03
+Activity factors‡	1.00 (Referent)	1.55 (1.05–2.29)	0.03
Adjustment for potential mediators			
+BMI§	1.00 (Referent)	1.53 (1.04–2.25)	0.03
+Health conditions‖	1.00 (Referent)	1.41 (0.95–2.10)	0.08
+BMI and health conditions	1.00 (Referent)	1.41 (0.95– 2.08)	0.09

BMI indicates body mass index; CHD, coronary heart disease; CI, confidence interval; and RR, relative risk.

*In addition to age, this model is further adjusted for diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/d), alcohol intake (0, 0.1–<5, 5–<15, 15–<30, ≥30 g/d, missing), and eating frequency (1–8 times a day).

†In addition to age and diet factors, this model is further adjusted for 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), and physical examination in last 2 years (yes/no).

‡In addition to age, diet and demographic factors, this model is further adjusted for activity factors: physical activity (quintiles of metabolic equivalent h/wk), television (asked in categories 0–1.5, 2.0–6.0, 7.0–20.0, ≥21.0 h/wk, missing), and sleep (<7, 7–8, >9 h/24 h, missing).

§In addition to age, 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 age, diet, demographic, and activity factors, this model is further adjusted for diabetes mellitus (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, body weight change, and specific dietary components such as folate, whole grains, fiber, or saturated fat did not substantially alter results.

with the original continuous versions of continuously gathered covariates yielded results similar to those obtained 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 1318 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 mellitus, 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 with men who ate 3 times a day, men who ate 1 to 2 times a day had a multivariate RR of 1.10 (95% CI, 0.92–1.32), whereas men who ate 4 to 5 times and ≥6 times a day had RRs of 1.05 (95% CI, 0.94–1.18) and 1.26 (95% CI, 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 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, body weight change every 4 years, and specific dietary components such as folate, whole grains, fiber, or saturated fat. Exclusion of participants with diabetes mellitus, 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 with men who ate breakfast, men who skipped breakfast had an RR of CHD of 1.48 (95% CI, 1.12–1.94) in models adjusted for only age, an RR of 1.40 (95% CI, 1.03–1.91) when further adjusted for diet and demographic and activity factors, and an attenuated RR of 1.34 (95% CI, 0.98–1.83) when additionally adjusted for the development of diabetes mellitus, hypertension, and hypercholesterolemia during follow-up. Results were unchanged when complete case analysis and multiple imputation were used 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 with participants who reported eating breakfast, those who did not answer the eating habits question had an RR of CHD of 1.02 (95% CI, 0.82–1.25). In stratified analyses, among men ≤60 years of age, those who skipped breakfast had a 50% higher risk of CHD compared with men who ate breakfast (multivariate RR, 1.55; 95% CI, 1.09–2.22), whereas this association was not significant in the older half of participants (RR, 1.06; 95% CI, 0.84–1.33; *P* for interaction=0.01; Table I in the online-only Data Supplement).

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 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 mellitus. 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]; eating habits have also been associated with incidence of diabetes mellitus[9] and total mortality.[29] It has previously been reported in the HPFS that compared with men who ate breakfast, participants who skipped breakfast were 15% more likely to have substantial weight gain (≥5 kg) during 10 years of follow-up[5] and were 21% more likely to develop type 2 diabetes mellitus.[9] Omitting breakfast has been reported to impair serum lipids and postprandial insulin sensitivity in multiple randomized, crossover trials.[6,30] A review of 8 randomized, controlled, crossover trials examining

Table 4. Eating Frequency and Multivariate RR of CHD With 95% CIs

	1–2 Times a Day	3 Times a Day	4–5 Times a Day	≥6 Times a Day
Cases, n	150	728	611	38
Person-years	39868	183947	155731	8408
Age-adjusted RR (95% CI)	1.17 (0.97–1.40)	1.00 (Referent)	1.08 (0.97–1.20)	1.30 (0.93–1.82)
+Diet factors*	1.13 (0.95–1.36)	1.00 (Referent)	1.06 (0.95–1.19)	1.26 (0.90–1.77)
+Demographic factors†	1.10 (0.92–1.32)	1.00 (Referent)	1.06 (0.95–1.19)	1.28 (0.91–1.79)
+Activity factors‡	1.10 (0.92–1.32)	1.00 (Referent)	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 (Referent)	1.03 (0.92–1.15)	1.25 (0.89–1.75)
+Health conditions‖	1.08 (0.90–1.30)	1.00 (Referent)	1.01 (0.90–1.13)	1.15 (0.82–1.61)
+BMI and health conditions	1.08 (0.90–1.29)	1.00 (Referent)	1.00 (0.89–1.11)	1.14 (0.81–1.61)

BMI indicates body mass index; CHD, coronary heart disease; CI, confidence interval; and RR, relative risk.

*In addition to age, this model is further adjusted for diet factors: diet quality (quintiles of alternate Healthy Eating Index 2010 score), energy intake (quintiles of kcal/d), and alcohol intake (0, 0.1–<5, 5–<15, 15–<30, ≥30 g/d, missing).

†In addition to age and diet factors, this model is further adjusted for 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), and physical examination in last 2 years (yes/no).

‡In addition to age, diet and demographic factors, this model is further adjusted for activity factors: physical activity (quintiles of metabolic equivalent h/wk), television (asked in categories 0–1.5, 2.0–6.0, 7.0–20.0, ≥21.0 h/week, missing), and sleep (<7, 7–8, >9 h/24 h, missing).

§In addition to age, 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 age, diet, demographic, and activity factors, this model is further adjusted for diabetes mellitus (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, body weight change, and specific dietary components such as folate, whole grains, fiber, or saturated fat did not substantially alter results.

the impact of eating habits without calorie restriction on CHD risk factors concluded that feasting (consuming all energy needs in 1 meal a day) was associated with higher low-density lipoprotein, apolipoprotein B, triglycerides, and blood pressure compared with nibbling (eating ≥3 times a day).[31] Eating frequency (times per day) in the HPFS has previously been reported to be associated with weight gain[5] and type 2 diabetes mellitus[9]; however, in the present analysis, we observed no association between frequency of eating and risk of CHD.

Table 5. Comparison of Eating Habits and Multivariate RR of Coronary Heart Disease With 95% CIs 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, times/d			
1–2	1.10 (0.91–1.31)	1.17 (0.86–1.58)	1.08 (0.79–1.47)
3	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
4–5	1.05 (0.94–1.18)	1.05 (0.79–1.38)	1.11 (0.84–1.47)
≥6	1.26 (0.90–1.77)	1.21 (0.56–2.61)	1.57 (0.72–3.42)

CI indicates confidence interval; and RR, relative risk. 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 examination in last 2 years, physical activity (metabolic equivalent h/wk), television (h/wk), and sleep hours (h/24 h).

*There are 97 fewer cases.

†The reference group is breakfast eaters.

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

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 behavior marker for several other lifestyle characteristics that may be related to CHD such as watching television,[35] engaging in physical activity,[36] or sleeping.[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 mellitus, BMI, and hypercholesterolemia, suggesting that eating habits may affect 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, whereas 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 cardiometabolic 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 measurements of circadian rhythms or light/dark exposure in our study, and the HPFS participants are not physicians, nurses, or other professionals who regularly work night shifts, so we were unable to examine how shift work influences eating habits. The present study had data only on regular eating habits, 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. Thus, 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 regular physical examinations 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 in terms of beverages such as sugar-sweetened beverages or alcoholic drinks, because these may not have been included in the eating frequency assessment when consumed without food. The eating habits question was asked only 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 homogeneous study population should reduce residual confounding as a result of unmeasured socioeconomic variability. The overall average diet quality of our study population was good, so it is not known whether 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.

Conclusions

We observed in this large, prospective study of middle-aged and older US male health professionals that breakfast eating was associated with a lowered risk of CHD. Our study is 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 to improve health at both the individual and population levels.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Among adults, skipping meals is associated with many cardiometabolic risk factors, including excess body weight, hypertension, insulin resistance, and elevated fasting lipid concentrations. However, no formal evidence-based dietary guidelines exist for adults concerning eating habits such as breakfast eating, and it has remained unknown whether specific eating habits regardless of dietary composition influence the 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 nonfatal 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 with men who ate breakfast, an association that was potentially a result of a combination of the mechanistic pathways of obesity, hypertension, hypercholesterolemia, and diabetes mellitus. 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 the best of our 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 to improve health at both the individual and population levels.

Prospective Study of Breakfast Eating and Incident Coronary Heart Disease in a Cohort of Male US Health Professionals

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SUPPLEMENTAL MATERIAL

Supplementary Table 1. Relative risk (RR) of coronary heart disease (CHD) with 95% confidence intervals (CI) for breakfast skippers and late night eaters stratified by updated risk factors.

		Skipping Breakfast*		Late Night Eating†	
	Person Time (%)	RR (95% CI)	Interaction p-value	RR (95%CI)	Interaction p-value
By Age					
≤ 60 Years old	35	1.55 (1.09, 2.22)	0.01	1.88 (0.81, 4.36)	0.79
> 60 Years old	65	1.06 (0.84, 1.33)		1.29 (0.83, 2.00)	
By Smoking Status					
Non-smoker	95	1.19 (0.97, 1.45)	0.41	1.31 (0.86, 2.00)	0.58
Current smoker	5	1.23 (0.60, 2.50)		6.71 (1.22, 36.75)	
By Alcohol					
< 5g/day	52	1.35 (1.05, 1.73)	0.46	1.98 (1.22, 3.20)	0.23
≥ 5g/day	48	1.03 (0.77, 1.39)		0.88 (0.42, 1.87)	

By Tertiles of Diet Quality					
1 (lowest)	33	1.45 (1.09, 1.93)		0.79 (0.34, 1.80)	
2	34	0.88 (0.62, 1.25)	0.62	1.31 (0.62, 2.77)	0.12
3 (highest)	33	1.19 (0.86, 1.63)		1.76 (0.92, 3.38)	
By Physical Activity					
< 15 MET hours/week	31	1.20 (0.88, 1.63)		1.66 (0.88, 3.14)	
15-30 MET hours/week	24	1.31 (0.89, 1.94)	0.82	1.32 (0.56, 3.09)	0.65
> 30 MET hours/week	45	1.18 (0.85, 1.63)		1.16 (0.58, 2.34)	
By Sleep					
< 7 hours/24 hours	16	1.36 (1.05,1.74)		1.71 (1.03, 2.85)	
7-8hours/24 hours	59	0.97 (0.58, 1.61)	0.50	1.35 (0.44, 4.14)	0.09
> 8 hours/24 hours	3	1.65 (0.25, 10.88)		0.35 (0.01, 10.91)	
By Television Watching					
≤ 1.5 hours/week	9	1.40 (0.60, 3.23)	0.23	0.65 (0.06, 7.09)	0.42
2-6 hours/week	37	1.18 (0.84, 1.66)		1.57 (0.80, 3.05)	

7-20 hours/week	42	1.27 (0.95, 1.71)		1.77 (0.93, 3.35)	
≥ 21 hours/week	12	1.72 (0.44, 6.64)		2.00 (0.50, 7.95)	
By BMI					
< 18.5	<0.05	‡		‡	
18.5 - < 25	41	0.98 (0.65,1.47)	0.99	1.81 (0.94, 3.51)	0.66
25 - < 30	47	1.18 (0.91,1.53)		1.52 (0.79, 2.95)	
≥ 30	12	1.39 (0.87, 2.22)		1.86 (0.69, 5.06)	
By Hypertension					
No	62	1.40 (1.07, 1.82)	0.13	1.85 (0.97, 3.52)	0.28
Yes	38	1.06 (0.81, 1.40)		1.12 (0.67, 1.87)	
By Hypercholesterolemia					
No	53	1.24 (0.92, 1.68)	0.53	1.80 (1.00, 3.23)	0.49
Yes	47	1.24 (0.97, 1.59)		1.29 (0.74, 2.24)	
By Diabetes					
No	93	1.21 (0.99, 1.49)	0.99	1.40 (0.91, 2.18)	0.87
Yes	7	1.46 (0.76, 2.81)		1.63 (0.49, 5.48)	

*Eating breakfast is the reference group for the skipping breakfast analysis.

†Not eating late at night is the reference group for the late night eating analysis.

‡Too small n to conduct analysis.

Multivariate model is adjusted for: age (months), 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), smoking (never, past, current, missing), marital status (yes, no, missing), full-time work status (yes, no, missing), physical activity (quintiles MET hours/week), physical exam in last two years (yes/no), 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), diabetes (yes/no), hypercholesterolemia (yes/no), hypertension (yes/no), parental myocardial infarction <60 years of age (yes/no), and BMI (<18.5, 18.5-24.9, 25-29.9, 30+ kg/m^2, missing) except for when stratified by one of these variables. Covariates were updated every 2 years unless they are dietary variables in which case they were updated every 4 years.