Eating Timing and Frequency as a Predictor of Hospitalization and/or Mortality From Coronary Artery Disease: The Linked CCHS-DAD-CMDB 2004-2013 Study

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ABSTRACT

Background: Coronary artery disease (CAD) is a major overlapping challenge in both clinical and public health realms due to high rates of hospitalization and mortality. Despite nutrition being a key risk factor for CAD, little is known about eating timing and frequency in Canadians or their relation to risk of hospitalization and/or mortality from CAD.

Methods: Breakfast consumption, between-meal consumption, eating frequency, and established CAD risk factors were assessed at baseline in 13,328 adults free of cancer and CAD from the 2004 Canadian Community Health Survey, Cycle 2.2. Nutrition Focus and were linked to administrative health databases to determine incidence of hospitalization and/or mortality from CAD in the following 9 years. Multivariable-adjusted hazard ratios with 95% confidence intervals estimated from Cox proportional hazards models were computed to

ORIGINAL ARTICLE

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RESUMÉ

Introduction : La maladie coronarienne (MC) est un enjeu majeur chevauchant les domaines clinique et de santé publique en raison des taux élevés d’hospitalisation et de mortalité. Bien que la nutrition soit un facteur de risque fondamental de la MC, on en connaît peu sur le moment et la fréquence de la consommation d’aliments chez les Canadiens ou sur leur relation au risque d’hospitalisation et/ou de mortalité en raison de la MC.

Méthodes : Nous avons initialement évalué la prise du déjeuner, la consommation entre les repas, la fréquence de la consommation d’aliments et les facteurs de risque établis de MC de 13 328 adultes indemnes de cancer et de MC de l’Enquête sur la santé dans les collectivités canadiennes de 2004, cycle 2.2. Volet nutrition, et avons lié les bases de données administratives en santé pour déterminer la fréquence d’hospitalisation et/ou de mortalité en raison de la MC dans

Cardiovascular disease is a leading cause of admission to the hospital, disability, and premature death, for both women and men in North America, causing an estimated economic burden of $351.3 billion in the US and $21.2 billion in Canada. Coronary artery disease (CAD) is the foremost cause of cardiovascular mortality and occurs as the result of a complicated cardiometabolic disease progression that begins with multiple potential overlapping risk factors. Diet has been identified as an important modifiable risk factor for CAD, and many previous dietary studies have established which foods and nutrients contribute to CAD morbidity and mortality prevention. However, little is known about the influence of the timing and/or frequency of consuming meals, snacks, and caloric beverages on CAD outcomes. To date, no evidence-based recommendations exist for adults regarding eating timing and/or frequency for CAD prevention, owing to a limited number of studies on the topic.

The prevalence of skipping breakfast has steadily increased among North American adults over the past decades,
test for associations between eating timing/frequency and hospitalization and/or mortality from CAD (n = 746 cases). **Results:** Skipping breakfast (12.0% of participants) and engaging in between-meal consumption (90.2%) were common practices, as was eating 4-5 times per day (55.2%). Skipping breakfast, between-meal consumption, and eating more or less than 4-5 times/day were strongly and bi-directionally associated with many sociodemographic, lifestyle, and metabolic risk factors at baseline. No associations were observed between skipping breakfast, between-meal consumption, or eating frequency and risk of hospitalization and/or mortality from CAD. **Conclusions:** Skipping breakfast, between-meal consumption, and eating frequency were associated with numerous established risk and preventative factors for CAD at baseline but were not directly associated with the risk of hospitalization and/or mortality from CAD in this cohort of Canadian adults.

alongside a parallel rise in snacking. These trends may have consequences at a population level, because accumulating evidence from short-duration trials, cross-sectional studies, and small prospective studies suggests that eating habits such as snacking and skipping meals are adversely associated with several biomarkers and cardiometabolic risk factors, including ghrelin secretion, weight gain, dyslipidemia, blood pressure, insulin resistance, and type 2 diabetes. Conversely, eating plans that involve intermittent fasting regimens (modifying eating timing and frequency patterns by engaging in periods of abstinence from food and caloric beverages) have been associated with improvements in insulin sensitivity, blood pressure, and blood lipid profiles in adults, and animal studies report that periods of fasting can improve metabolic health indicators and counteract disease processes. However, evidence on the long-term effects of these eating plans on cardiometabolic health outcomes is limited. Skipping breakfast, which is often defined as the first meal of the day that breaks the fast after the longest period of sleep and occurs within 2 to 3 hours of awakening, is a common component of some intermittent fasting methods. Of note, long-term human intervention studies of eating plans that involve fasting are rare, because of ethical and feasibility reasons. The few prospective cohort studies of eating timing and frequency and risk of incident CAD events (such as a myocardial infarction) reported inconclusive results, although the topic has not yet been researched among solely the most extreme cases causing hospitalization and mortality, or in a Canadian population. Definitions of eating timing and frequency patterns (breakfast, eating occasions, snacks, and meals) and CAD varied across these studies, making comparison among them difficult. To add to the controversy over whether these eating and frequency patterns can have beneficial or detrimental health effects, several potential confounding factors, such as sociodemographic and lifestyle factors, cannot yet be ruled out as influencers of the relationship between eating timing and frequency patterns and cardiometabolic health. The objectives of our study were as follows: (i) to characterize the eating timing and frequency patterns, including skipping breakfast, between-meal consumption, and eating frequency, in a Canadian cohort of diverse socioeconomic status with publicly funded healthcare; and (ii) to prospectively determine whether skipping breakfast, eating infrequently, and between-meal consumption were associated with long-term increased or decreased risk of hospitalization and/or mortality from CAD in this cohort.

**Methods**

**Data sources and study population**

The dataset analyzed in the present study was the linked Canadian Community Health Survey-Discharge Abstract Database-Canadian Mortality Database 2004-2013 (CCHS-DAD-CMDB), which is a population-based dataset probabilistically linked using birthdate, sex, and postal code information by Statistics Canada for the probabilistically linked using birthdate, sex, and postal code information by Statistics Canada for the 9 years following. As previously described, Statistics Canada allows researchers access to this CCHS-DAD-CMDB dataset at their Research Data Centres, which are secure computing facilities that house Statistics Canada’s confidential microdata; researchers can apply for access to de-identified data files for analysis. Participants included in the linked dataset provided consent to share and link their data to administrative health data.
Detailed descriptions of the sampling strategy, recruitment process, design, and methods of the CCHS 2.2 have been published previously. Briefly, the CCHS 2.2 targeted people of all ages who were living in private dwellings in the 10 Canadian provinces. The survey is representative of 98% of the Canadian population living in the provinces but did not include full-time members of the Canadian Armed Forces or people living in the territories, on First Nations Reserves or Crown Lands, in institutions, or in some remote areas. The sample was designed to be representative of the Canadian population in terms of age, sex, geography, and socioeconomic status. The survey consisted of 2 components: a 24-hour dietary recall (a subsample of ~31% of participants completed a second 24-hour dietary recall 3 to 10 days later) and a general health questionnaire that collected information on sociodemographic characteristics, chronic conditions, anthropometric measures, physical activity, alcohol consumption, and smoking, among other variables. Trained Statistics Canada personnel conducted the computer-assisted interviews in-person on all days of the week (including weekend days) in the participants’ homes. The Discharge Abstract Database (DAD) is maintained by the Canadian Institute of Health Information (CIHI) and contains information on diagnoses, treatment, length of stay, and discharge status for all individuals admitted to the hospital in all provinces except Quebec. The Canadian Mortality Database (CMDB) is a census of all registered deaths in Canada that includes the underlying and supporting cause and date of death and demographic information, such as name, date of birth, and postal code at the time of death. Deaths occurring in Canada are reported by the provincial and territorial Vital Statistics Registers to Statistics Canada and are then entered into the CMDB.

Participants were excluded from the present analysis if they were <18 years old, were residents of Quebec (due to a lack of corresponding hospitalization data in the DAD), had self-reported prevalent heart disease at baseline, had self-reported cancer at baseline, reported implausible energy intakes of <500 or >5000 kcal per day, as is a common practice in nutrition studies, or did not provide consent to share their survey information with provincial and federal ministries of health and to link their responses to administrative health data. After exclusions, the final sample size was 13,328 CCHS 2.2 participants. Statistics Canada granted ethical approval and access to the de-identified linked dataset for the present project (under project number 18-SSH-DAL-5581), and all analyses were conducted at the Atlantic Research Data Centre.

Eating patterns and other dietary assessment

Dietary intake data were collected using a modified version of the US Department of Agriculture Automated Multiple-Pass Method (AMPMM) for 24-hour dietary recall, which is an automated 5-step computerized recall method that uses multiple memory cues to maximize a participant’s ability to recall all foods eaten in the previous 24 hours. For each food and beverage item reported, participants were asked to self-define the eating occasion and time of food consumption by answering the following 2 questions: (i) “What would you call this eating occasion? Breakfast, lunch (dinner), supper (dinner), brunch, between-meal consumption, drink, extended consumption, other”; and (ii) “About what time did you begin to eat/drink food item(s)?” The time of food consumption was indicated according to the 24-hour clock. In this study, we defined breakfast consumption as a positive response to breakfast or brunch. Breakfast, lunch, supper, and brunch were considered meals, whereas snacks, drinks (containing calories), extended consumption (eating or drinking was continuous throughout the day), and other were combined and considered between-meal consumption. Consumption of a food or beverage item (except plain drinking water) was considered a separate eating occasion if it was separated in time from the preceding and succeeding reported eating occasion by at least 60 minutes, a time interval that has been used previously to distinguish eating occasions. We totaled the number of meals and between-meal consumption occasions reported by each participant to calculate eating frequency.

Nutrient and energy intakes for each participant (covariates in the present study) were calculated by Statistics Canada using the Canadian Nutrient File, version 2001b, which is a computerized, bilingual food composition database containing average values for nutrients in foods commonly consumed in Canada.

Measurement of covariates

Information on sociodemographic characteristics (age, sex, marital status, education, food security, household income before taxes), lifestyle and mental health factors (physical activity index, smoking status, alcohol intake, life stress), and health conditions (high blood pressure, diabetes) was collected by using the general health questionnaire component of the CCHS 2.2. Total daily energy expenditure values (kcal/kg per day) were used to calculate a physical activity index (“active” = ≥3.0 kcal/kg per day, “moderate” = 1.5-2.9 kcal/kg per day, “inactive” = <1.5 kcal/kg per day). Body mass index (BMI) was calculated by dividing participants’ weight in kilograms by their height in metres squared (kg/m²); <18.5, 18.5-24.9, 25-29.9, ≥30). Diagnoses of high blood pressure and diabetes were self-reported by the participant.

CAD hospitalization and/or death ascertainment

Hospitalization and cause-of-death information was coded using the Canadian version of the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10-CA) in the 9-year follow-up period. Specifically, participants with ICD-10-CA codes of 121, 122, 124, and 125 from the DAD and CMDB, and Canadian Classification of Health Interventions codes 1.IJ.76, 1.IJ.50, 1.IJ.55, and 1.IJ.57 from the DAD, were identified as a case of hospitalization and/or mortality from CAD. We also conducted a sensitivity analysis in which we added hospitalization and/or mortality from angina (ICD-10-CA code I20) to the outcome definition. Data were not available on cases of CAD that did not require hospitalization or result in death. All diagnoses (not only primary diagnoses) were included. Participants were observed for up to 9 years and contributed follow-up time from the date they participated in the CCHS 2.2 until the date of first documented hospitalization and/or death from CAD, date of death from non-CAD causes, or end of the follow-up period (March 31, 2013), whichever came first.
Statistical analysis

We used Stata 16.1 software (StataCorp, College Station, TX) to conduct all statistical analyses, according to an analysis plan developed a priori. All analyses were conducted at a 2-tailed alpha level of 0.05. We chose to analyze the data using a cohort-based approach, and therefore all analyses were unweighted. To investigate the validity of a single administration of a 24-hour dietary recall to measure eating timing and frequency, we used Cohen’s kappa statistic to assess the agreement of the first 24-hour dietary recall with the CCHS 2004’s second 24-hour recall, which was conducted on a subsample of individuals (~30% of participants). We grouped participants based on breakfast-eating status (yes, no) and summarized baseline characteristics, comparing the 2 groups using Student t tests or Wilcoxon rank-sum tests for continuous variables, and \( \chi^2 \) tests for categorical variables. We also summarized baseline characteristics according to eating frequency (total eating occasions per day; \( \leq 3 \), 4-5, \( \geq 6 \)), comparing the 3 groups using 1-way analysis of variance or Kruskal-Wallis tests for continuous variables, and \( \chi^2 \) tests for categorical variables.

To quantify the risk of incident hospitalization and/or mortality from CAD associated with eating patterns, we used stepwise multivariable-adjusted Cox proportional hazard regression models to estimate adjusted hazard ratios and 95% confidence intervals (CIs). The proportional hazards assumption was verified using Schoenfeld residuals. In the basic multivariate model 1, we adjusted for age (years) and sex. In multivariate model 2, we adjusted for the following demographic factors: predominant racial group (white [yes, no]); immigrant (yes, no, missing); marital status (married/common-law, not married/common-law [widowed, separated, divorced, single, never married], missing); education (\( \leq \) secondary school graduation, > secondary school graduation, missing); food security (secure, insecure, missing); household income before taxes (< $15,000, $15,000-$29,999, $30,000-$49,999, $50,000-$79,999, \( \geq \) $80,000, missing). In multivariate model 3, we further adjusted for the following baseline lifestyle and mental health factors: smoking (never, past, current, missing); alcohol intake (0-3 times per month, 1-3 times per week, 4+ times per week, missing); physical activity index (active, moderately active, inactive, missing); and life stress (not at all stressful, not very stressful, a bit stressful, quite a bit or extremely stressful, missing). In multivariate model 4 (our main model reported for this study), we further adjusted for the following baseline dietary factors: consumption of sugar-sweetened beverages (yes, no); fruit and vegetable intake (total number of times per day); energy intake (kcal per day); and eating frequency (times per day). High blood pressure (yes, no, missing), diabetes (yes, no, missing), and BMI (kg/m\(^2\), 18.5-24.9, 25-29.9, \( \geq \) 30, missing) are potential mediators and were adjusted for in subsequent Cox regression models to test whether our results were materially altered by their inclusion. This method of examining potential mediation was used in previous studies of eating timing and frequency. 30,32,41,42 In models in which eating frequency was the main exposure, we also adjusted for breakfast (yes, no). Values were coded as “missing” if they were unavailable at baseline (< 1% for most covariates; < 10%-14% for household income and BMI).

Results

In this cohort of 13,328 adults (> 20% of whom were aged \( \geq \) 65 years at baseline), 1597 (12.0%) reported skipping breakfast on the day of the 24-hour dietary recall (Table 1), and 1301 (9.8%) reported no between-meal consumption. Of participants, 2497 (18.7%) reported eating \( \leq 3 \) times, 7357 (55.2%) reported eating 4-5 times, and 3474 (26.1%) reported eating \( \geq 6 \) times (Table 2). We found fair agreement between the two 24-hour dietary recalls with respect to breakfast consumption (percent agreement: 86.5%, Cohen’s kappa: 0.33, standard error: 0.02), between-meal consumption (percent agreement: 83.7%, Cohen’s kappa: 0.22, standard error: 0.02, and eating frequency (percent agreement: 53.4%, Cohen’s kappa: 0.22, standard error: 0.01). Breakfast-nonconsumer and breakfast-consumer groups significantly differed in all the 27 baseline variables compared. Of note, breakfast skippers had higher frequencies of some well-established CAD risk factors, such as smoking, not being in the major racial group (white), food insecurity, less dietary fibre intake, more sugar-sweetened food intake, and less education than participants who reported that they ate breakfast. Breakfast skippers also were younger (median of 33 years vs 49 years), were less likely to be an immigrant, consumed fewer calories, and had a lower frequency of hypertension or diabetes. Between-meal consumption and eating frequency were similarly associated with many baseline variables that are known to both increase and decrease risk of CAD. For example, participants who reported between-meal consumption also reported higher levels of stress, alcohol intake, and physical activity compared to those who did not report between-meal consumption. Eating frequency was inversely associated with food insecurity, alcohol intake, and male sex, and directly associated with fibre intake, physical activity, and being in a married/common-law relationship.

During 9 years of follow-up, 746 CAD-related hospitalizations and/or deaths were documented. No association was observed between skipping breakfast and risk of hospitalization and/or mortality from CAD (hazard ratio [HR] = 1.00, 95% confidence interval [CI]: 0.71-1.40) in any of the models (Table 3). Likewise, no association was observed between between-meal consumption and risk of hospitalization and/or mortality from CAD (HR 1.03, 95% CI: 0.79-1.34; Table 3). We also did not observe an association between eating frequency and risk of CAD hospitalization and/or mortality (Table 4); compared with participants who ate \( \leq 3 \) times per day, participants who ate 4-5 times per day had a multivariable HR of 0.94 (95% CI: 0.71-1.25), and participants who ate \( \geq 6 \) times per day had an HR of 0.84 (95% CI: 0.50-1.41). Including hospitalization and/or mortality from angina in our outcome definition resulted in an additional 30 cases (n = 776) but did not materially alter our results (Supplemental Tables S1 and S2).

Discussion

To the best of our knowledge, our study is the first to characterize eating timing and frequency in a Canadian cohort and assess whether skipping breakfast, between-meal consumption, and eating frequency are prospectively related to an increased risk of hospitalization and/or mortality from CAD. In this large prospective study of a Canadian cohort with 9
Table 1. Characteristics of the 2004 Canadian Community Health Survey (CCHS): nutrition participants at baseline, by breakfast consumption status and between-meal consumption status

| Characteristics                          | Breakfast consumption | Between-meal consumption | P     |
|-----------------------------------------|-----------------------|--------------------------|-------|
| Age, y                                  | 33 (22, 48)           | 49 (31, 66)              | < 0.001 |
| Sex                                     | < 0.001               |                          |       |
| Male                                    | 836 (52.4)            | 4974 (42.4)              | 584 (44.9) |
| Female                                  | 761 (47.7)            | 6757 (57.6)              | 717 (55.1) |
| Immigrant to Canada                     | 186 (11.7)            | 1871 (16.0)              | < 0.001 |
| Largest racial group (white)            | 269 (16.8)            | 1345 (11.5)              | < 0.001 |
| No                                      | 1327 (83.1)           | 10,380 (88.5)            | 1126 (86.6) |
| Urban residence                         | 1247 (78.1)           | 8885 (75.7)              | 1005 (77.3) |
| Food insecure                           | 197 (12.3)            | 778 (6.6)                | < 0.001 |
| Current smoker                          | 730 (45.7)            | 2704 (23.1)              | < 0.001 |
| Alcohol use, times per wk               |                       |                          | < 0.001 |
| None                                    | 249 (15.6)            | 2538 (21.6)              | 371 (28.5) |
| < 1                                     | 703 (44.0)            | 4775 (40.7)              | 495 (38.1) |
| 1–3                                     | 505 (31.6)            | 3106 (26.4)              | 325 (25.0) |
| 4+                                     | 139 (8.7)             | 1306 (11.1)              | 108 (8.3) |
| Self-perceived stress                   |                       |                          | < 0.001 |
| Not at all stressful                    | 329 (20.6)            | 2024 (17.3)              | 232 (17.8) |
| Not very stressful                      | 344 (2.9)             | 233 (19.9)               | 237 (19.7) |
| A bit stressful                         | 174 (10.9)            | 1473 (12.6)              | 215 (16.5) |
| Quite a bit stressful*                 | 376 (23.5)            | 2940 (25.1)              | 356 (27.4) |
| Extremely stressful*                    | 946 (59.2)            | 6459 (55.1)              | 764 (58.7) |
| Married/common-law                      | 376 (23.5)            | 2904 (25.1)              | 303 (23.3) |
| Household income, $                     | 606 (38.0)            | 5940 (50.6)              | < 0.001 |
| < 15,000                                | 181 (11.3)            | 1179 (10.1)              | 167 (12.8) |
| 15,000–29,999                           | 273 (17.1)            | 2225 (19.0)              | 270 (20.8) |
| 30,000–49,999                           | 354 (22.2)            | 2494 (21.3)              | 285 (21.9) |
| 50,000–79,999                           | 333 (20.9)            | 2647 (22.6)              | 259 (19.9) |
| ≥ 80,000                                | 276 (17.3)            | 2110 (18.0)              | 174 (13.4) |
| Missing                                 | 180 (11.3)            | 1076 (9.2)               | 146 (11.2) |
| Education                               |                       |                          | < 0.001 |
| < Secondary school graduation           | 403 (25.2)            | 2840 (24.2)              | 421 (32.4) |
| Secondary school graduation             | 388 (24.3)            | 2232 (19.0)              | 252 (19.4) |
| Some postsecondary                     | 247 (15.5)            | 1157 (9.9)               | 109 (8.4) |
| Postsecondary graduation                | 543 (34.0)            | 5411 (46.1)              | 507 (39.0) |
| BMI, kg/m²                               | 25.7 (22.8, 29.7)     | 26.2 (23.1, 29.9)        | 0.033 |
| < 18.5                                  | 41 (2.6)              | 205 (1.8)                | 30 (2.3) |
| 18.5–24.9                               | 567 (35.5)            | 4015 (34.2)              | 419 (32.2) |
| 25–29.9                                 | 480 (30.1)            | 3718 (31.7)              | 412 (31.7) |
| ≥ 30                                    | 333 (20.9)            | 2560 (21.8)              | 298 (22.9) |
| Missing                                 | 176 (11.0)            | 1233 (10.5)              | 142 (10.9) |
| High blood pressure                     | 155 (9.7)             | 2290 (19.5)              | 270 (20.8) |
| Diabetes                                | 54 (3.4)              | 765 (6.5)                | 5 (3.8) |
| Energy intake, kcal/d                   | 1729.0 (1233.2, 2447.3) | 1846.4 (1369.9, 2462.4) | < 0.001 |

Continued
Table 1. Continued.

| Characteristics                          | No (n = 1597) | Yes (n = 11,731) | No (n = 1301) | Yes (n = 12,027) | P   |
|-----------------------------------------|---------------|------------------|---------------|------------------|-----|
| BMI, body mass index                     | BMI, body mass index | BMI, body mass index | BMI, body mass index | BMI, body mass index | P   |
| 4.5 (3.6)                               | 4.3 (3.5)     | < 0.001          | 4.3 (3.5)     | 4.3 (3.5)        | 0.001 |
| 5.3 (4.6)                               | 5.1 (4.4)     | 0.001            | 5.1 (4.4)     | 5.1 (4.4)        | 0.001 |
| Between-meal consumption                 | 1495 (93.6)   | 10532 (89.8)     | N/A           | N/A              | < 0.001 |
| Fruits and vegetables, times/d           | 2.7 (1.7, 3.9) | 3.9 (2.7, 5.3)   | < 0.001       | < 0.001          | < 0.001 |
| Consumed a sugar-sweetened beverage      | 795 (49.8)    | 4028 (34.3)      | < 0.001       | < 0.001          | < 0.001 |
| Sodium, mg/d                            | 2543.1 (1629.6, 3716.2) | 2693.2 (1862.6, 3785.3) | 18.8 (11.2, 29.8) | 20.0 (12.7, 30.2) | < 0.001 |
| Sugar, g/d                              | 79.0 (44.1, 129.5) | 88.2 (55.7, 133.4) | 60.3 (42.5, 93.4) | 64.0 (44.4, 107.5) | < 0.001 |
| Fiber intake, g/d                       | 19.2 (11.7, 30.7) | 22.0 (16.7, 30.5) | 17.4 (12.2, 23.4) | 15.5 (10.3, 24.2) | < 0.001 |
| Protein intake, g/d                     | 66.2 (42.9, 90.0) | 79.9 (53.3, 107.9) | 62.4 (41.9, 92.0) | 67.4 (43.4, 95.2) | < 0.001 |
| Carbohydrate intake, g/d                | 21.3 (14.1, 29.4) | 22.0 (16.7, 30.5) | 17.4 (12.2, 23.4) | 15.5 (10.3, 24.2) | < 0.001 |

Values are displayed as mean (standard deviation) or median (interquartile range) for continuous variables and, or n (%) for categorical variables unless otherwise indicated.

BMI, body mass index; N/A, not applicable.* Quite a bit stressful and extremely stressful were combined due to low cell count.
death, meaning we captured the more severe cases of CAD only. This possibility potentially explains our observation of no significant association between skipping breakfast and hospitalization and/or mortality from CAD.

Another potential explanation for the lack of association between eating timing and frequency patterns and risk of hospitalization and/or mortality from CAD in this study is that eating timing and frequency may be too strongly aligned with other diet-related (eg, food insecurity or diet quality) or CAD-related factors (eg, BMI, hypertension) to assess it independently in this cohort. Eating timing and frequency were associated with both established risk factors and...
Table 3. Breakfast and between-meal consumption and multivariable-adjusted hazard ratios (HRs) of hospitalization and/or mortality from coronary artery disease with 95% confidence intervals (CIs)

|                          | Breakfast |        |        |        |
|--------------------------|-----------|--------|--------|--------|
|                          | No        | Yes    | P      |
| Cases, n                 | 40        | 706    |        |
| Person-years             | 13,514.5  | 96,564.0 |      |
| Adjusted for age and sex: | 1.15 (0.83–1.60) | 1.00 (Ref) | 0.399 |
| Demographic factors†    | 1.13 (0.81–1.57) | 1.00 (Ref) | 0.473 |
| + Lifestyle and mental health factors† | 1.01 (0.72–1.40) | 1.00 (Ref) | 0.965 |
| + Dietary factors†       | 1.00 (0.71–1.40) | 1.00 (Ref) | 0.993 |
| Additional adjustment for potential mediators |        |        |        |
| + Health conditions†     | 1.01 (0.72–1.41) | 1.00 (Ref) | 0.971 |
| + BMI†                   | 1.01 (0.72–1.41) | 1.00 (Ref) | 0.969 |

### Between-meal consumption

|                          | No        | Yes    | P      |
|--------------------------|-----------|--------|--------|
| Cases, n                 | 87        | 659    |        |
| Person-years             | 10,518.6  | 99,560.0 |      |
| Adjusted for age and sex: | 1.00 (Ref) | 1.08 (0.87–1.35) | 0.489 |
| Demographic factors†    | 1.00 (Ref) | 1.08 (0.87–1.36) | 0.477 |
| + Lifestyle and mental health factors† | 1.00 (Ref) | 1.05 (0.84–1.32) | 0.664 |
| + Dietary factors†       | 1.00 (Ref) | 1.03 (0.79–1.34) | 0.834 |
| Additional adjustment for potential mediators |        |        |        |
| + Health conditions†     | 1.00 (Ref) | 1.03 (0.79–1.34) | 0.831 |
| + BMI†                   | 1.00 (Ref) | 1.03 (0.79–1.33) | 0.853 |

Boldface indicates the main model being reported.

BMI, body mass index; Ref, referent.

† In addition to age (years) and sex (male, female), this model is adjusted for the following baseline demographic factors: largest racial group (yes, no); marital status (married, not married); education (≤ secondary school graduation, > secondary school graduation, missing); immigrant (yes, no, missing); food secure (yes, no, missing); and household income (< $15,000, $15,000–$29,999, $30,000–$49,999, $50,000–$79,999, ≥ $80,000, missing).

‡ In addition to age, sex, and baseline demographic factors, this model is further adjusted for the following baseline lifestyle and mental health factors: smoking (never, past, current, missing); alcohol intake (none < 3 times per month, 1–3 times per week, 4+ times per week, missing); physical activity index (active, moderately active, inactive, missing); and life stress (not at all stressful, not very stressful, a bit stressful, quite a bit or extremely stressful, missing).

§ In addition to age, sex, baseline demographic, lifestyle, and mental health factors, this model is further adjusted for the following baseline dietary factors: consumption of sugar-sweetened beverages (yes, no); fruit and vegetable intake (times per day); eating frequency (times per day); sodium (mg per day), sugar (g per day); and energy intake (kcal per day). This is the main model reported for this analysis.

∥ In addition to age, sex, and baseline demographic, lifestyle, mental health, and dietary factors, this model is further adjusted for baseline health conditions: high blood pressure (yes, no, missing); and diabetes (yes, no, missing).

* In addition to age, sex, baseline demographic, lifestyle, and mental health factors, this model is further adjusted for the following baseline dietary factors: sodium (mg per day), sugar (g per day); and energy intake (kcal per day). This is the main model reported for this analysis.

preventative factors for CAD at baseline in our study, and these factors could be neutralizing the association between eating timing/frequency and risk of hospitalization and/or mortality from CAD. For example, the mean age of participants reporting that they did not eat breakfast (33 years) was substantially lower than the mean age of participants reporting that they ate breakfast (49 years). Potentially, people with metabolic risk factors, such as older age, high BMI, hyperglycaemia, hypertension, or hypercholesterolemia, are more likely to adopt practices generally regarded as “healthy,” such as eating breakfast and eating regularly, which could generate a reverse causation type effect such as indication bias.

### Limitations and strengths

Our study had several limitations that should be noted. First, misclassification bias may have been present because breakfast consumption, between-meal consumption, and eating frequency were assessed at one point in time via a single administration of a 24-hour dietary recall, which does not capture daily variation or measure habitual dietary intake or patterns. However, we compared the responses of participants who completed both the initial and second 24-hour dietary recalls (n = 3986) and found fair agreement between the 2 recalls with respect to breakfast consumption, between-meal consumption, and eating frequency. Eating timing and frequency patterns may have changed within the 9-year follow-up period; therefore, nondifferential misclassification error may have been present, which would have attenuated true associations. Differential misclassification bias could have also been present if participants who were at high risk of CAD changed their eating habits in response to advice from a healthcare provider during the follow-up period. Second, we cannot rule out possible residual confounding by unknown or unmeasured factors (eg, bodyweight change, familial hypercholesterolemia, sedentary behaviour, shift work, circadian rhythms, light/dark exposure, and sleep pattern). Third, covariates were measured at baseline only; therefore, we were unable to adjust for time-varying confounders. Fourth, the CCHS 2.2 data were not linked to physician billing databases, which provide records of insured services provided by physicians in each province, or insured patient registries, which record longitudinal information regarding the entire population of insured beneficiaries of provincial healthcare services,
including date of immigration to or emigration from Canada. Therefore, we were unable to assess the relationship between eating frequency and timing and cases of CAD not requiring hospitalization or causing death, or censor CCHS 2.2 participants who emigrated from Canada during the follow-up period at the date of emigration. Fifth, the duration of follow-up was relatively short in the present study and may have presented insufficient incubation time for capturing hospitalization and mortality from CAD in this population. Therefore, whether associations exist between eating timing and frequency and CAD hospitalization and/or mortality in the longer-term is unknown.

Despite these limitations, our study has several strengths, including a prospective design, a large Canadian sample within a public healthcare system, a large sample of women (who have historically been underrepresented in epidemiologic and clinical CAD research\(^5,5^2\)), exclusion of prevalent CAD, inclusion of a wide range of socioeconomic and health statuses, minimal missing data, and comprehensive assessment of various demographic, lifestyle, dietary, and health-related factors, which we were able to control for in our Cox regression models.

**Future directions**

The present study has analyzed the available Canadian data and identified that additional prospective cohort and clinically based longitudinal studies that enroll participants of diverse demographics are needed to confirm the findings of the present study and further elucidate these relationships at different age points. Although such studies are time- and resource-intensive, they are needed to elucidate potential mechanisms linking eating timing and frequency with hospitalization and/or mortality from CAD, and they also would enable the analysis of repeated measures of eating timing and frequency during the follow-up period. Future studies should attempt to capture usual eating timing and frequency repeatedly, in addition to food and nutrient intake, and they should explore the agreement and error associated with repeated measures of eating timing and frequency over time, as these have not yet been available to study in any dataset. Future studies of eating timing and frequency should attempt to account for other potential confounders and effect modifiers during follow-up time, such as bodyweight change, sedentary behaviour, shift work, circadian rhythms, light/dark exposure, and sleep pattern. An effort to link the CCHS 2.2 data with other population-based administrative health databases such as physician billing databases and insured patient registries also should be made to allow for the capture of cases of CAD that did not result in hospitalization and/or mortality. Future studies also should examine eating timing and frequency in relation to other cardiometabolic outcomes, such as hypertension, dyslipidemia, and stroke, which may have different etiologic pathways.

**Conclusions**

We observed in this population-based prospective longitudinal cohort study that consuming breakfast, between-meal consumptions, and eating 4-5 times per day are common eating patterns among Canadian adults and are linked to
higher socioeconomic status and a healthier lifestyle. We did not detect an association between eating timing and frequency (measured as skipping breakfast, between-meal consumption, and eating frequency) and risk of hospitalization and/or mortality from CAD in this population. However, the relationships between eating timing and frequency, and socioeconomic, demographic, lifestyle, and mental health factors are multi-directional and complex, and the direct associations between eating timing and frequency patterns and hospitalization and/or mortality from CAD may have been offset by the interplay of these factors. Replication in other long-term studies representing diversity in participant socioeconomic characteristics is needed, as are more repeated and validated assessments of usual eating timing and frequency in nutrition studies.

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Disclosures
The authors have no conflicts of interest to disclose.

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**Supplementary Material**

To access the supplementary material accompanying this article, visit CJ C Open at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2022.03.011.