Associations of number of daily eating occasions with type 2 diabetes risk in the Women’s Health Initiative Dietary Modification Trial

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WHI data collections tools, data dictionary, the protocol and instructions for data use requests are available at www.whi.org

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Abbreviations:
BMI: Body mass index
DGA: Dietary Guidelines for Americans
DPP: Diabetes Prevention Program
HEI: Healthy Eating Index
NDS: Nutrition Data Systems
NSES: neighborhood socioeconomic status
24HR: 24-hour recall
T2D: Type 2 diabetes
WHI: Women’s Health Initiative
WHI-DM: Women’s Health Initiative Dietary Modification Trial
Abstract

Background: Over 23 million Americans have type 2 diabetes (T2D). Eating habits such as breakfast consumption, time-restricted eating and limiting daily eating occasions have been explored as behaviors for reducing T2D risk, but prior evidence is inconclusive.

Objective: To examine associations between number of daily eating occasions and T2D risk in the Women’s Health Initiative Dietary Modification Trial (WHI-DM) and whether associations vary by body mass index (BMI), age, or race/ethnicity.

Methods: Participants were postmenopausal women in the WHI-DM who comprised a 4.6% subsample completing 24-hour dietary recalls (24HR) at years 3 and 6 as part of trial adherence activities (n=2,159). Numbers of eating occasions/day were obtained from the year 3 24HR and participants were grouped into approximate tertiles as 1-3 (n=795), 4 (n=713) and ≥5 (n=651) daily eating occasions as the exposure. Incident diabetes was self-reported on semi-annual questionnaires as the outcome. WHI-DM is registered at clinicaltrials.gov (NCT00000611).

Results: Fifteen percent (15.4%, n=332) of the WHI-DM 24HR cohort reported incident diabetes at follow-up Cox proportional hazards regression tested associations of eating occasions with T2D adjusted for neighborhood socioeconomic status (NSES), BMI, waist circumference, race/ethnicity, family history of T2D, recreational physical activity, Healthy Eating Index (HEI)-2005, 24HR energy intake and WHI-DM arm. Compared to women reporting 1-3 meals/day, those consuming 4 meals/day had a T2D HR=1.38 (95%CI 1.03-1.84) without further increases in risk for ≥5 meals/day. In stratified analyses, associations for 4 meals/day compared to 1-3 meals/day were stronger in
women with BMI <30.0 kg/m² (HR=1.55, 95% CI 1.00-2.39) and women ≥ age 60 (HR=1.61, 95% CI 1.11-2.33).

**Conclusions:** 4 daily meals/day compared to 1-3 meals/day was associated with increased risk of T2D in postmenopausal women, but no dose-response effect was observed for additional eating occasions. Further studies are needed to understand eating occasions in relation to T2D risk.

**Introduction**

The prevalence of Type 2 diabetes mellitus (T2D) is very high in the United States (1), and is projected to nearly triple over the coming decades (2). According to the Centers for Disease Control and Prevention (CDC), more than 23 million Americans have T2D, which is the seventh leading cause of death in the U.S. (1). T2D is a serious public health problem due to the associated significant comorbidities and medical complications. In 2017, expenditures for T2D and related complications were estimated at $327 billion dollars (3, 4).

T2D is a preventable disease. Genetic susceptibility influences risk of T2D, but modifiable lifestyle habits such as body weight, diet and physical activity are equally, if not more important risk factors (5-7). The Diabetes Prevention Program (DPP) Clinical Trial demonstrated that individuals at increased risk of T2D who were randomized to an energy- and fat-restricted dietary intervention reduced T2D incidence by more than 50% compared to control (8, 9). Further, the Look AHEAD study demonstrated that an intensive weight loss/lifestyle intervention was associated with continuous sustained partial or complete remission of T2D for up to 4 years (10). Other dietary-modification
approaches include consumption of healthy dietary patterns (6) and reducing dietary glycemic load (11, 12).

Eating behaviors such as regular breakfast consumption, time-restricted eating (eating only during specific hours of the day) and the number of daily eating occasions have emerged as potential, but not confirmed, independent factors influencing T2D risk (13-16). There is no consensus as to whether eating frequency increases or decreases risk, independent of associations with weight management. Chronic exposure to hyperglycemia, which could occur with more frequent eating episodes, damages pancreatic β-cell function leading to impaired glucose regulation and increased T2D risk (17). The scientific and clinical dilemma is whether mildly elevated glucose throughout the day that accompanies frequent eating is more (or less) detrimental with regards to T2D risk compared to larger glucose oscillations that occur following sizeable but less frequent meals (14, 18-22). Research examining total eating occasions as an independent and modifiable risk factor for T2D may help address this question. Therefore, our objective was to evaluate the relationship between the number of daily eating occasions and T2D risk in the Women’s Health Initiative Dietary Modification Clinical Trial (WHI-DM) and whether these associations varied by participant characteristics such as BMI, age or race/ethnicity. We hypothesized that eating more times throughout the day would be associated with increased risk of T2D.

Methods

The design, recruitment and data collection methods of the Women’s Health Initiative Dietary Modification Trial (WHI-DM) have been previously described (23, 24). Briefly, from 1993-98, 48,835 postmenopausal women from 40 U.S. clinical centers
were randomized to a low-fat dietary pattern (n= 19,541, 40%) or a comparison/usual diet group (n=29,294, 60%) using a permuted block algorithm with blocks of size 5, 10 or 15 and stratified by clinical center and baseline age group (50-54-, 55-59-, 60-69- and 70-79-years-old). The intervention was a behavioral modification program designed to lower fat intake to 20% of total energy and to increase fruit and vegetable and grain servings to at least 5 and 6 servings per day, respectively. Neither energy intake restrictions nor weight loss goals were intervention components. The primary trial outcomes were breast and colorectal cancer and a secondary outcome was coronary heart disease. While T2D was not a designated primary or secondary outcome, the low-fat high fruit and vegetable diet intervention did not increase the risk for T2D and may have slowed progression (T2D was not an exclusion for WHI-DM participation) (25, 26).

The WHI-DM protocol and all procedures were approved by the institutional review boards at each of the 40 clinical centers and at the WHI Clinical Coordinating Center. All women signed written informed consent. WHI is registered at clinicaltrials.gov as NCT00000611.

WHI-DM participants attended baseline clinic visits where standardized questionnaires on personal and family medical history of major chronic diseases, current and past smoking history, recreational physical activity (usual frequency and duration of recreational physical activity such as walking, biking and computed as MET hours/week) (27), self-reported race/ethnicity, education (categorical with options ranging from less than high school completion to advanced and professional degrees), income (categorical) and other demographic and lifestyle characteristics were completed as part of the WHI protocol (24). Clinic staff measured waist circumference,
height and weight using standardized study protocols and body mass index (BMI) was computed as weight(kg)/height(m).²

**Dietary Assessment**

Dietary intake for the WHI-DM was monitored primarily by a food frequency questionnaire (FFQ) designed for the WHI (28). The FFQ was administered to all participants during screening (baseline), one year after randomization, and thereafter annually to one-third of the participants on a rotating basis. Baseline dietary data examined for this analysis included daily intake of energy, added sugars, total sugars and computed Healthy Eating Index 2005 (HEI-2005) scores, which measures adherence to the Dietary Guidelines for Americans (DGA) (29). HEI-2005 is on a scale of 1-100 where a higher score reflects greater adherence to DGA. The WHI-DM also included a 4.6% subsample of participants who provided one 24-hour dietary recall (24HR) at both years 3 and 6 (but not at WHI-DM enrollment/baseline) as part of trial adherence activities. The year 3 24HRs are used in the analysis in this report to create a measure of eating frequency, as food frequency questionnaires lack data on meal composition and meal timing. Selection to the WHI 24HR cohort was achieved using sampling stratified on clinic, age and race/ethnicity. Women from race/ethnic minority groups were oversampled for the 24 HR cohort because the WHI scientific goals included having the statistical power for race/ethnic-specific analyses of trial response (23, 24). The 24HR were collected by trained interviewers who used the USDA multiple pass method (30) and the Nutrition Data Systems (NDS) software (Nutrition Coordinating Center, University of Minnesota). Quality assurance was performed and 10% of all 24HR records were reviewed by a Registered Dietitian supervisor.
The 24HR data are well-suited for studying meal timing and the number of daily meals since discrete eating occasions and time of consumption are collected as part of the recall record. The 24HR protocol included collection of all meals and snacks for foods and beverages consumed the previous day. The number of daily eating occasions was calculated by summing the number of distinct occasions recorded in the recall record as the variable MEALNAME in NDS: Breakfast, Lunch, Dinner, Snack(s). For this analysis, eating occasions were defined in 30-minute increments such that 30 minutes between recorded eating episodes was recorded as a new eating event. Participants were grouped into approximate tertiles according to their eating occasion totals: 1-3/day, 4/day and ≥5/day.

Outcomes

Prevalent diabetes was documented by self-report at the WHI baseline visit by asking each participant if she has ever been told by a physician that she has “sugar diabetes” when not pregnant. Incident T2D during follow-up was documented by self-report at each semiannual contact when participants were asked: “Since the date given on the front of this form, has a doctor prescribed any of the following pills or treatments?” Response options included “pills for diabetes” and “insulin shots for diabetes.” The self-report for these medications was previously shown to be very consistent with medication inventories (31, 32). During the trial period follow-up through 2005, 18.6% of all WHI-DM participants were diagnosed with T2D. For this analysis we excluded those with either any reported T2D prior to the cohort entry time at WHI-DM year 3 as well as those diagnosed within the first three years of follow-up.
**Statistical analysis**

The 24HR cohort began recalls in Year 3 (WHI-DM baseline and year 1 used Four Day Food Records for adherence and retention activities), so the 24HR cohort (n=2,460) entry date was designated as WHI-DM year three. Exclusions for analysis included 24HR energy intake <600 kcals or >5000 kcals (n=49), as these were considered unreliable intakes, baseline history of self-reported diabetes (n=142), incident diabetes between recall cohort start date and 12 months later (n=91), and loss to follow-up (n=19) leaving n=2,159 for analysis. Missing data for covariates were all less than 1% with the exception of neighborhood socioeconomic status (n=201, 9.3%) and recreational physical activity (n=255, 11.8%). Participants with missing data drop out of multivariate adjusted models.

Cox proportional hazards regression was used to examine the relationship across the tertiles of eating occasions and risk of T2D. *A priori* subgroup analyses examined these associations stratified by baseline BMI (<30.0/≥30.0 kg/m²) race/ethnicity and age. The WHI-DM was one of the first dietary intervention trials to have specific minority recruitment goals as well as goals to achieve a broad distribution across the range of the postmenopausal years (33). This heterogeneity has enabled many subgroup analyses not possible without this heterogeneity (for example, (34-36) and supports the *a priori* subgroups for this analysis. All models were adjusted for neighborhood socio-economic status (NSES) (37), race/ethnicity, BMI, waist circumference, recreational physical activity, family history of diabetes,, self-reported energy intake from the 24HR, time between study enrollment and recall administration,
HEI-2005 and WHI trial arm assignment. Models are intended to be parsimonious to avoid overfitting; therefore, variables without evidence of confounding in this study sample, such as smoking were not included. All tests were two-sided and P<0.05 was considered statistically significant. Statistical analyses were conducted in Stata (StataCorp LLC. College Station, TX).

Results

The characteristics of the study sample by tertiles of eating occasions are presented in Table 1. Fifteen percent (15.4%, n=332) of the sample reported incident diabetes after the start of the recall cohort. Compared to the referent (1-3 eating occasions per day), women reporting 4 daily eating occasions had a multivariate-adjusted diabetes HR =1.38 (95% CI 1.03-1.84) (Table 2). Among women reporting 5 or more eating occasions per day the multivariate-adjusted HR was attenuated and not statistically significant (HR=0.95, 95% CI 0.70-1.29).

We next examined whether BMI, race/ethnicity or age influenced the eating occasions-diabetes risk associations in stratified analyses (Table 3). Women with BMI <30 kg/m² who reported 4 eating occasions/day had a significantly increased risk of diabetes (HR=1.55, 95% CI 1.00-2.39) compared to those reporting 1-3 meals/day. However, among women with BMI ≥ 30 kg/m² the number of daily eating occasions had no apparent relationship to diabetes risk. Older (≥60 years), but not younger, women who reported 4 eating occasions per day had nearly a 60% greater risk for diabetes (HR=1.61, 95% CI 1.11-2.33) compared to those reporting 1-3 eating occasions per day. Associations of eating occasions with T2D risk did not differ by race/ethnicity.
Discussion

In the Women’s Health Initiative Dietary Modification Trial, participants who reported 4 daily eating occasions had a 36% increased risk of incident diabetes compared to those reporting 1-3 daily eating occasions. These associations were stronger in women with BMI < 30 kg/m² or in women ≥60 years of age. No additional increase in risk was found for higher daily eating occasions (≥5/day) and no dose-response was detected. We are not certain why the results became attenuated and null for >5 eating occasion/day and we cannot rule out chance as a reason for any of the findings. It is possible that the participants with >5 eating occasions per day represents a heterogeneous phenotype because the range of eating occasions in this tertile was 5-10. Combining into a single group could have masked other characteristics that we are unable to discern at this time.

The hypothesis for this study was based on the following biological rationale. Eating multiple times throughout the day keeps blood glucose and insulin at mildly elevated levels but with lower peaks and troughs, effectively demonstrated by Munsters et al (38). Importantly, insulin resistance, which is known to escalate with age (39, 40), may increase the irregularity in circulating glucose, supporting our finding in women over 60 years of age. Further, a constant postprandial state that accompanies multiple eating occasions places excess stress on the pancreas while continued insulin secretion prevents the secretion of counterregulatory hormones. Animal models consistently demonstrate metabolic advantage and reduced metabolic stress in mice consuming kcal-controlled and time-controlled eating (41). Recent studies of intermittent
Fasting in humans suggest that meal restriction may benefit metabolic health and diabetes risk (22, 42-44). In contrast, other research findings have reported metabolic advantages with more, not less, frequent eating. Jenkins et al. conducted a randomized crossover trial in 17 overweight men (45). Participants in one arm consumed provided foods on an outpatient basis three times daily (termed the ‘meals’ phase). On the other arm, the same foods were divided into 17 energy- and macronutrient-equivalent portions and participants were instructed to consume one food packet per hour (termed the ‘nibbling’ phase). Serum insulin and C-peptide were substantially and significantly lower following the nibbling phase compared to the meals phase. Heden et al. reported that the incremental area under the curve for insulin was significantly larger following a three meal per day experimental condition in eight obese women compared to a six meal per day condition (21). We previously reported a randomized crossover trial comparing meals (eating 3 times per day) to grazing (eating 8 times per day) (46). A Registered Dietitian gave detailed guidance to study participants as they prepared and consumed their own meals throughout the two study periods. The protocol specified that total energy and macronutrient distribution were to be kept constant on both study arms. We found that compared to the grazing pattern, the meals pattern led to significantly higher serum IGF-1, which is secreted in response to an insulin stimulus (46). Taken together, the data to date are not consistent.

Behavioral factors may account for our findings in this WHI report. It is possible that those who limit eating occasions to 1-3 times per day (referent group) have less emotional and binge eating levels. In the Diabetes Prevention Program (DPP), higher scores on food cravings, binge eating and episodic overeating were linked with higher
baseline BMI, which is a strong risk factor for T2D (47). We were not able to specifically evaluate these eating behavioral measures as these were not part of the WHI-DM trial data collection protocol.

Few prospective studies on total eating occasions in healthy volunteers at average risk of T2D have been conducted. The Nurses’ Health Study examined breakfast consumption and skipping breakfast, but not eating occasions per se not eating occasion per se as a goal (14). However, one of their subgroup analyses found no association of number of daily eating occasions with T2D risk (14). In the Health Professionals’ Follow-Up Study, a similar analysis focused primarily on breakfast consumption also included a subgroup analysis incorporating both breakfast consumption and number of meals per day (15). The association of 4-7 meals per day with increased risk of T2D was strongest among those who reported no breakfast (15). Both the Health Professionals and Nurses’ Health Studies inquired about breakfast on separate questionnaires. WHI did not explicitly inquire about breakfast consumption so we are not able to perform a similar analysis. Other published studies have primarily examined inclusion or omission of a specific meal on T2D risk (48), and there remains a paucity of data on whether fewer, or greater overall eating occasions per day is associated with higher or lower T2D risk. Numerous studies, including randomized controlled trials (20) have examined the optimal number of daily eating occasions for management of existing T2D, but we are unaware of additional prospective studies aimed at understanding dietary behavioral risk factors for subsequent diagnosis of T2D.

This report focused on examining whether a modifiable risk factor, the number of eating occasions per day was associated with T2D risk. We recognize that analysis of
daily eating occasions is notoriously difficult due to problems with methodology and meal definitions (49). In this study we used the eating occasions as reported on the 24 HR recall record. Some studies have used a single question with unknown validity on how many meals are consumed daily (49). Other complexities in studying eating occasions relates to diet quality; foods and beverages commonly consumed, as “snacks” tend to have a less favorable nutrient profile and higher energy density (e.g., fats and sweets, baked goods, dairy-based desserts, chips, cookies, and crackers) (50, 51). Increased frequency of intake is also highly correlated with overall energy intake and weight gain – both risk factors for T2D (51-54). Randomized controlled trials testing low vs. high eating frequency while maintaining eucaloric energy as well as comparable macronutrient distribution and diet quality are well-suited to testing whether the number of eating occasions affects metabolic health (21, 55). However, such studies are usually short term and typically employ surrogate endpoints (e.g., biomarkers, weight) as outcomes instead of disease endpoints; cohort studies such as WHI afford the opportunity to test these important associations with confirmed disease endpoints.

The strengths of this study include embedding the analysis in a randomized controlled trial, trained interviewers who followed a standardized protocol to collect the 24HR data, a diverse study sample, and carefully collected disease endpoints. Additionally, the WHI-DM 24HR cohort was designed to have higher race/ethnicity diversity than the overall WHI-DM. Limitations include the use of one 24HR, which we recognize may not reflect usual dietary patterns or eating frequency habits. No consensus exists on whether eating frequency occasions should be any reported eating occasion, minimal kcal thresholds, time intervals or other criteria (49). We used a 30-
minute interval between reported eating occasions to allow enough time for completion
of an eating occasion in this postmenopausal age group. An alternative approach could
have used 15 minute intervals as used in some other studies (49, 56, 57). Another
limitation is that we were not able to assess the nutritional quality of specific foods
because these 24HR were collected prior to the routine inclusion of food group data in
the 24HR output. The lack of technical ability to map eating occasions with specific
foods could have affected the interpretation of the findings across the tertiles of eating
occasions. Furthermore, since the 24HR cohort was a 4.6% subsample of the WHI-DM,
results may not pertain to all WHI participants. Another limitation is that all studies of
dietary self-report are subject to misreporting and measurement error, including the WHI
(58, 59). While we have not specifically examined measurement error in this study,
others have reported measurement error in reporting of eating frequency and that such
measurement error may influence eating frequency-disease association outcomes (60, 61).
Finally, with all studies, uncontrolled confounding may occur when potential
confounding variables are either not measured or not measured with precision.

In conclusion, data from the WHI Dietary Modification Trial suggest that eating 4
times per day compared to 1-3 times per day is associated with a 38% higher risk of
T2D, but no association was observed when daily eating occasions equaled or
exceeded five times per day, possibly due to too much variation in the top tertile (5-10
eating occasions/day). The risk was shown to be slightly stronger among women with a
BMI <30.0 kg/m² (55% higher risk) or in women ≥ 60 years of age (61% higher risk).
Since our results are not entirely consistent with our hypothesized dose-response
association, future cohort studies would be informed by including biomarkers of insulin
resistance that would provide more definitive evidence on whether the total number of daily eating occasions is or is not associated with risk of T2D.

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Table 1. Baseline characteristics of participants in the Women’s Health Initiative Dietary Modification Trial with available 24-hr dietary recall data at year 3, by number of eating occasions per day (n=2159)

| Characteristic                          | Number of eating occasions per day |
|----------------------------------------|------------------------------------|
|                                        | 1–3 (n = 795)                      |
|                                        | 4 (n = 713)                        |
|                                        | 5+ (n = 651)                       |
| **Mean ±SD or N (%)**                  |                                    |
| Demographics                           |                                    |
| Age (y)                                | 62.6 ± 6.7                         |
|                                        | 62.0 ± 6.8                         |
|                                        | 60.4 ± 6.5                         |
| NSES¹                                 | 73.1 ± 10.5                        |
|                                        | 74.6 ± 9.3                         |
|                                        | 75.2 ± 8.8                         |
| Race/ethnicity                         |                                    |
| Non-Hispanic white                     | 420 (52.8)                         |
|                                        | 434 (60.9)                         |
|                                        | 428 (65.8)                         |
| Black                                  | 220 (27.7)                         |
|                                        | 145 (20.3)                         |
|                                        | 91 (14.0)                          |
| Hispanic                               | 72 (9.06)                          |
|                                        | 53 (7.43)                          |
|                                        | 50 (7.68)                          |
| Asian / Pacific Islander               | 48 (6.04)                          |
|                                        | 47 (6.59)                          |
|                                        | 60 (9.22)                          |
| Other / unknown                        | 35 (4.40)                          |
|                                        | 34 (4.77)                          |
|                                        | 22 (3.38)                          |
| Anthropometry                          |                                    |
| Weight (kg)                            | 78.0 ± 17.5                        |
|                                        | 75.0 ± 15.1                        |
|                                        | 74.3 ± 16.0                        |
| Body mass index (kg/m²)                | 29.8 ± 6.3                         |
|                                        | 28.6 ± 5.2                         |
|                                        | 28.3 ± 5.4                         |
| Waist circumference (cm)               | 89.7 ± 13.8                        |
|                                        | 87.7 ± 12.6                        |
|                                        | 86.4 ± 12.9                        |
| Physical activity (MET-hr/wk)          | 10.2 ± 13.1                        |
|                                        | 9.7 ± 10.8                         |
|                                        | 10.6 ± 12.7                        |
| Current Smoking (yes)                  | 47 (6.0)                           |
|                                        | 44 (6.3)                           |
|                                        | 42 (6.5)                           |
| Family history of diabetes³            | 277 (37.4)                         |
|                                        | 247 (36.5)                         |
|                                        | 242 (38.9)                         |
| Current Smoking (yes)                  | 47 (6.0)                           |
|                                        | 44 (6.3)                           |
|                                        | 42 (6.5)                           |
| Family history of diabetes³            | 277 (37.4)                         |
|                                        | 247 (36.5)                         |
|                                        | 242 (38.9)                         |
| Dietary intake²                        |                                    |
| Energy (kcal/d)                        | 1753 ± 731                         |
|                                        | 1772 ± 693                         |
|                                        | 1831 ± 723                         |
| Total sugar (g/d)                      | 94.0 ± 45.7                        |
|                                        | 96.2 ± 44.5                        |
|                                        | 98.1 ± 45.3                        |
| Added sugar (g/d)                      | 51.8 ± 35.3                        |
|                                        | 51.2 ± 31.1                        |
|                                        | 53.6 ± 33.5                        |
| Diet quality (HEI-2005)                | 63.2 ± 10.3                        |
|                                        | 64.1 ± 10.3                        |
|                                        | 64.0 ± 9.5                         |
| Energy from 24-hr recall (kcal)        | 1431 ± 495                         |
|                                        | 1568 ± 523                         |
|                                        | 1648 ± 510                         |

¹ NSES = neighborhood socioeconomic status  
² Baseline intake assessed by food frequency questionnaire  
³ Type 2 diabetes
Table 2. Associations of daily eating occasions with incident diabetes in the Women’s Health Initiative Dietary Modification Trial

| Eating frequency | n events / total (%) | Model 1<sup>1</sup> | Model 2<sup>2</sup> |
|------------------|----------------------|----------------------|----------------------|
|                  | HR (95% CI)          | HR (95% CI)          |                      |
| 1–3 times/day    | 117/795 (14.7)       | 1.0 (ref)            | 1.0 (ref)            |
| 4 times/day      | 129/713 (18.1)       | 1.18 (0.92 - 1.51)   | 1.38 (1.03 - 1.84)   |
| 5+ times/day<sup>3</sup> | 86/651 (13.2) | 0.80 (0.61 - 1.06) | 0.95 (0.70 - 1.29) |

1. Model 1 adjusted for age
2. Model 2 adjusted for age, NSES, race/ethnicity, BMI, waist circumference, energy intake from 24-hr recall, family history of type 2 diabetes, physical activity, HEI-2005, time between baseline and 24-hr recall, and WHI clinical trial arm(s)
3. range -5-10 times/day
Table 3. Associations of daily eating occasions with incident diabetes in the Women’s Health Initiative Dietary Modification Trial, stratified by BMI**, race/ethnicity and age*  

| Eating frequency | BMI < 30 kg/m² | | | BMI ≥ 30 kg/m² | |
|---|---|---|---|---|---|
| | n events / total (%) | HR (95% CI) | | n events / total (%) | HR (95% CI) | |
| 1–3 times/day | 43 / 461 (9.33) | 1.0 (ref) | | 74 / 331 (22.4) | 1.0 (ref) | |
| 4 times/day | 71 / 460 (15.4) | 1.55 (1.00 - 2.39) | | 58 / 251 (23.1) | 1.14 (0.76 - 1.69) | |
| 5+ times/day¹ | 42 / 428 (9.81) | 0.80 (0.47 - 1.34) | | 44 / 222 (19.8) | 0.72 (0.45 - 1.14) | |
| Non-Hispanic white | | | | All other race/ethnicities | |
| 1–3 times/day | 50 / 420 (11.9) | 1.0 (ref) | | 67 / 375 (17.9) | 1.0 (ref) | |
| 4 times/day | 66 / 434 (15.2) | 1.45 (0.95 - 2.21) | | 63 / 279 (22.6) | 1.26 (0.85 - 1.89) | |
| 5+ times/day¹ | 47 / 428 (11.0) | 0.71 (0.43 - 1.15) | | 39 / 223 (17.5) | 0.86 (0.52 - 1.41) | |
| Age < 60 y | | | | Age ≥ 60 y | |
| 1–3 times/day | 49 / 268 (18.3) | 1.0 (ref) | | 68 / 527 (12.9) | 1.0 (ref) | |
| 4 times/day | 46 / 268 (17.2) | 1.13 (0.71 - 1.82) | | 83 / 445 (18.7) | 1.61 (1.11 - 2.33) | |
| 5+ times/day¹ | 45 / 319 (14.1) | 1.06 (0.48 - 1.32) | | 41 / 332 (12.4) | 0.77 (0.47 - 1.24) | |

* Models are adjusted for age, NSES, race/ethnicity, waist circumference, physical activity, family history of type 2 diabetes, HEI-2005, HEI-2005, energy intake from 24-hr recall, time between baseline and 24-hr recall, and clinical trial arm(s)  

** BMI <30 kg/m² combines normal and overweight; BMI ≥30.0 kg/m² is obese.  
¹ Range -5-10 times/day