



# The Impact of Eating Frequency and Time of Intake on Nutrient Quality and Body Mass Index: The INTERMAP Study, a Population-Based Study



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## ABSTRACT

**Background** Epidemiologic evidence is sparse on the effect of dietary behaviors and diet quality on body mass index (BMI; calculated as  $\text{kg}/\text{m}^2$ ), which can be important drivers of the obesity epidemic.

**Objective** This study investigated the relationships of frequency of eating and time of intake to energy density, nutrient quality, and BMI using data from the International Study on Macro/Micronutrients and Blood Pressure including 2,696 men and women aged 40 to 59 years from the United States and the United Kingdom.

**Design** The International Study on Macro/Micronutrients and Blood Pressure is a cross-sectional investigation with four 24-hour dietary recalls and BMI measurements conducted between 1996 and 1999. Consumption of solid foods was aggregated into eating occasion. Nutrient density is expressed using the Nutrient Rich Food Index 9.3. The ratio of evening/morning energy intake was calculated; mean values of four visits were used.

**Statistical analyses performed** Characteristics across eating occasion categories are presented as adjusted mean with corresponding 95% CI. Multiple linear regression models were used to examine associations of eating occasions, ratio of evening/morning energy intake, dietary energy density, and Nutrient Rich Food Index 9.3 with BMI.

**Results** Compared to participants with fewer than four eating occasions in 24 hours, those with six or more eating occasions in 24 hours had lower mean BMI (27.3 vs 29.0), total energy intake (2,129 vs 2,472 kcal/24 hours), dietary energy density (1.5 vs 2.1 kcal/g), and higher Nutrient Rich Food Index 9.3 (34.3 vs 28.1). In multiple regression analyses, higher evening intake relative to morning intake was directly associated with BMI; however, this did not influence the relationship between eating frequency and BMI.

**Conclusions** Our results suggest that a larger number of small meals may be associated with improved diet quality and lower BMI. This may have implications for behavioral approaches to controlling the obesity epidemic.

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OVERWEIGHT AND OBESITY HAVE INCREASED globally in both men and women over the last 30 years.<sup>1</sup> Evidence indicates that overweight is caused primarily by environmental factors, particularly adverse dietary and other lifestyle habits.<sup>2</sup> Adiposity is an established risk factor for morbidity and mortality, primarily from diabetes, cardiovascular diseases, and cancers.<sup>3,4</sup> Data are sparse on the role of dietary behaviors and energy density as important drivers of the obesity epidemic; for example, frequency of eating and time of meals and how these relate to body weight.<sup>5,6</sup> Previous studies on associations of eating frequency and body weight have yielded inconsistent results. Some studies reported that more frequent intake throughout the day is associated with lower body mass index (BMI; calculated as  $\text{kg}/\text{m}^2$ ),<sup>7-9</sup> and others found no association.<sup>10,11</sup> As for the time of energy intake, prospective cohort studies found that shift workers are at

higher risk of developing coronary heart disease and type 2 diabetes, reflecting consumption of a large proportion of their energy during the night.<sup>12,13</sup> However, the impact of a greater energy load in the evening vs the morning has not been thoroughly explored. Evidence suggests that a reduction in dietary energy density<sup>14</sup> and increased nutrient density<sup>15</sup> are favorable for weight management. Here we explore associations between number of eating occasions and time of energy intake on dietary energy density, nutrient density, and BMI.

## METHODS

### Population Sampling and Study Design (1996 to 1999)

The International Study on Macro/Micronutrients and Blood Pressure (INTERMAP) is a cross-sectional epidemiologic

investigation of macronutrients, micronutrients, and blood pressure/adiposity. Study design and methods have been described previously.<sup>16</sup> A total of 4,680 men and women aged 40 to 59 years were recruited randomly from community and workforce populations stratified by age and sex from 17 population samples in four countries (Japan, the People's Republic of China, United States, and the United Kingdom). Here, we present data on participants from eight population samples in the United States and two population samples in the United Kingdom. Country-specific metabolic phenotype of this study had been investigated using proton nuclear magnetic resonance spectroscopy.<sup>17</sup> This methodology identifies metabolic profiles that discriminate across populations. Hierarchical cluster analysis of nuclear magnetic resonance spectra showed similar urinary metabonomic profiles of US and UK populations, suggesting participants from the United States and United Kingdom had similar dietary intakes.<sup>17</sup> Of the 2,724 US and UK individuals, data on 128 who did not attend all four visits, presented unreliable dietary data, or had incomplete data or violated protocol were excluded. Unreliable dietary data were identified when a serving size and key nutrients presented unusual values, and total energy intake was exceptionally high or low (<500 kcal/24 hours or >5,000 kcal/24 hours for women and 8,000 kcal/24 hours for men), with no reasonable explanation.<sup>16</sup> In addition, we used sex-specific Schofield equations<sup>18</sup> to determine basal metabolic rate, and energy expenditure was calculated at "low" physical activity level (1.4) for adults.<sup>19</sup> Therefore, we also excluded data on 311 individuals who possibly under-reported energy intake based on a ratio of energy intake to estimated energy expenditure <95% confidence limit.<sup>20</sup> All analyses presented here are based on data from 2,385 participants (1,232 men and 1,153 women). Each participant gave written informed consent and attended four clinic visits. Institutional ethics committees approved the study at all sites. The study was approved by Institutional Review Boards at Northwestern University as STU00024158 and National Research Ethics Service, Committee London—Fulham as EC3169.

### Dietary Assessment

Four standardized 24-hour dietary recalls were collected from each participant using the multipass method by trained dietary interviewers.<sup>16</sup> Two recalls were on consecutive days and two on consecutive days approximately 3 weeks later. Each participant provided two timed 24-hour urine collections between the first and second study visits and the third and fourth study visits. Data were entered using a computerized database in the United States (Nutrition Data System, version 2.9, 1996, University of Minnesota).<sup>21</sup> In the United Kingdom, data entry was done using standard forms, then coded and computerized. For each country, national food composition tables were used to calculate nutrient content of all reported foods and beverages. Tables were standardized across countries and validated by the Nutrition Coordinating Center, University of Minnesota.<sup>21,22</sup> For nutrients supplying energy, intake was calculated as percentage total energy (% kcal), and for others, as intake per 1,000 kcal; nutrients were calculated also as amounts per 24 hours. Measurements were averaged across the four study visits for dietary variables. All nutrient data here are exclusive of supplement intake. Mean amount of solid food intake was calculated for

each participant as food weight (g/24 hours). Mean amount of beverages was calculated for each participant as beverage weight (g/24 hours). To assess validity of dietary recalls, population sample and sex-controlled correlations between dietary and urinary total protein, sodium, and potassium were calculated,<sup>21</sup> with correlation coefficients of 0.52, 0.46, and 0.58, respectively, for United States and 0.48, 0.36, and 0.51, respectively, for United Kingdom. Selected food groups were identified and included whole-fat and low-fat/medium-fat dairy products, red meats, fish and shellfish, raw vegetables, cooked vegetables, fruits (excluding juices), cakes, and sweet pies; averaged over four visits and expressed in g/1,000 kcal.

### Frequency of Eating

We estimated frequency of eating by defining an eating occasion as any instance in which participants reported consumption of solid meals and snacks, with a minimum gap of 15 minutes between occasions. This time gap was adopted from previous studies on eating frequency<sup>8</sup> and allows capture of main meal intake as well as snacks. We excluded all beverages including water, fruit juice, soda, alcoholic beverages, tea, and coffee from the eating occasion counts to avoid overestimation of the total number of eating occasions per 24 hours. If a participant had, for example, a cup of tea between meals, that would not be considered an eating occasion. We classified eating occasions into the following categories: <4, ≥4 to <5, ≥5 to <6, and ≥6/24 hours.

### Time and Place of Intake

Times and places of eating were reported by participants during each 24-hour dietary recall. We expressed time of intake as the ratio of evening/morning energy intake. Morning intake was defined as mean energy intake from 6:00 AM to 11:55 AM, and evening intake was defined as mean energy intake from 6:00 PM to 11:55 PM. These times were selected based on when the majority (98%) of the US and UK INTERMAP participants consumed morning and evening meals. We classified participants into quartiles of the ratio of evening/morning energy intake (<1.0, ≥1.0 to <1.5, ≥1.5 to <2.0, ≥2.0). Places of meal intake included home, work, school, restaurant, friend's home, during travel, and other.

### Dietary Energy Density

We calculated energy density of the diet as total energy intake divided by total weight of solid food consumption per visit. Mean energy density over four visits was used in the analyses. Only solid foods were included in calculating energy density, consistent with previous studies that concluded that beverages should be excluded.<sup>23</sup> This is because the lower density of liquids compared to solid food can result in disproportionate individual energy density values, which can affect associations of outcomes with the energy density variable.<sup>23</sup>

### Nutrient Density

We used the Nutrient Rich Food Index 9.3 (NRF9.3) as a measure of nutrient quality of individual foods and the nutrient density of the overall diet.<sup>24</sup> The NRF9.3 has previously been validated against the Healthy Eating Index,<sup>25</sup> an established measure of diet quality based on the 2005

Dietary Guidelines for Americans<sup>26</sup> and MyPyramid.<sup>27</sup> Unlike other methods to assess nutrient quality of the diet, this index includes the sum of daily values of nine nutrients to encourage (ie, protein; dietary fiber; vitamins A, C and E; calcium; iron; potassium and magnesium) minus the sum daily values for nutrients to limit (ie, saturated fat, added sugar and sodium) based on 100 kcal.  $NRF9.3 = (\text{protein g}/50 + \text{fiber g}/25 + \text{vitamin A IU}/5,000 + \text{vitamin C mg}/60 + \text{vitamin E IU}/30 + \text{calcium mg}/1,000 + \text{iron mg}/18 + \text{magnesium mg}/400 + \text{potassium mg}/3,500 - \text{saturated fat g}/20 - \text{added sugars g}/50 - \text{sodium mg}/2,400) \times 100$ . Higher NRF9.3 indicate higher nutrient density per 100 kcal; participants with a high NRF9.3 were considered to have a healthier diet than those with a low NRF9.3.

### Assessment of Body Mass Index

Weight and height were measured twice without shoes or heavy clothes on the first and third visit. BMI was calculated as weight (kg)/height (m<sup>2</sup>). We classified participants according to their BMI level as normal (BMI  $\leq 24.9$ ), overweight (25.0 to  $< 29.9$ ), or obese ( $\geq 30.0$ ).

### Lifestyle Factors

During two visits, interviewers used questionnaires to obtain data on daily alcohol intake during the previous 7 days (mean alcohol intake over 14 days, expressed as g/24 hours, was used in all analyses), cigarette smoking (yes/no), education level (years of completed education), physical activity (hours per day engaged in moderate physical activity, eg, walking) and heavy physical activity (eg, running) during leisure time as reported by participants, on a special diet (eg, energy restricted diet for the purpose of weight reduction) at the time of the study (yes/no), and dietary supplement use (yes/no).

### Statistical Methods

BMI, eating occasions, ratio of evening/morning energy intake, energy density, NRF9.3, food weight, and beverage weight were averaged over four visits for each participant.

Reliability of BMI and eating occasions (mean of four visits) was estimated from the formula  $1/[1+(\text{ratio}/2)] \times 100$ , where the ratio is intra-individual variance/inter-individual variance, estimated separately by sex, and for women and men combined. It was calculated from means of the first two and second two visits to account for higher correlation between values on consecutive days. The reliability of eating occasion gives a first approximation of effect of random error (day-to-day variability) on size of eating occasion associations with BMI. The statistic is estimated size of an observed coefficient as percent of theoretical coefficient in univariate regression analysis.<sup>28</sup>

Characteristics across eating occasion categories are presented as adjusted mean with corresponding 95% CIs applying the generalized linear model. Models were adjusted sequentially for potential dietary and lifestyle cofounders (total energy intake, sex, age, educational level, hours engaged in moderate and heavy physical activity, smoking, on a special diet, dietary supplement use, and population sample).

We used multiple linear regression models adjusted for total energy, sex, age, and population samples (eight US samples and two UK samples) to examine associations of eating occasions, ratio of evening/morning energy intake, dietary energy density, and NRF9.3 with BMI. Regression

coefficients were calculated as kg/m<sup>2</sup> for two standard deviation differences in eating occasions, ratio of evening/morning energy intake, dietary energy density, and NRF9.3. Sensitivity analyses were done using adjusted multiple linear regression models for two subcohorts, excluding those after a weight-loss diet, those diagnosed with diabetes mellitus, and/or cardiovascular disease. Bonferroni correction method was applied to denote statistical significance. Analyses were performed using SAS (version 9.3, SAS Institute Inc).

### RESULTS

Descriptive baseline characteristics for the total 2,385 INTERMAP US and UK participants are presented in Table 1. Mean BMI, total energy intake, and dietary energy density were higher in men compared to women. Mean eating occasions were slightly higher for women than men. The NRF9.3 was higher in women compared to men. Univariate estimates of reliability of eating occasion based on mean values from the four 24-hour recalls/participant, ranged from about 71% to 76% of the theoretical coefficient, and were similar for men and women. The reliability estimate for BMI was 99.8% overall; estimates were similar across population samples and by sex (data not shown).

### Eating Occasions

Participants with  $\geq 6$  eating occasions/24 hours consumed higher amounts of solid foods, had greater intakes of low/medium-fat dairy products, fruits ( $P$  for trend  $< 0.0001$ ), raw and cooked vegetables ( $P$  for trend = 0.02), and lower intakes of alcohol and red meats ( $P$  for trend  $< 0.0001$ ) compared to those with  $< 4$  eating occasions/24 hours (Table 2). Adjusted mean BMI was lower for those with  $\geq 6$  eating occasions/24 hours compared to those with  $< 4$  eating occasions/24 hours.

### Time of Intake

Participants with  $< 1.0$  compared with  $\geq 2.0$  ratio of evening/morning energy intake had lower total energy intake and dietary energy density; significantly lower alcohol intake and higher NRF9.3 (Table 3, available online at [www.andjrn.org](http://www.andjrn.org)).

### Eating Occasions and Time of Intake

The median ratio of evening/morning energy intake (1.8) was used to categorize low and high evening energy consumption. Table 4 showed that participants who ate more frequently and consumed most of their energy earlier in the day ( $\geq 6$  eating occasions/24 hours and ratio of evening/morning energy intake  $\leq 1.8$ ) had lower energy density, total energy intake, and alcohol intake; higher NRF9.3, food weight, and fruit intake compared to those who ate fewer eating occasions/24 hours and consumed most of their food later in the day ( $< 4$  eating occasions/24 hours and ratio of evening/morning energy intake  $> 1.8$ ).

In addition, information on meal location show that 26%, 33%, 25%, and 16% of participants with  $< 4$ ,  $\geq 4$  to  $< 5$ ,  $\geq 5$  to  $< 6$ , and  $\geq 6$  eating occasions/24 hours, respectively, were having their evening meals at restaurants/cafeterias (data not shown).

### Multiple Regression Analyses

In multiple regression analyses, BMI was inversely associated with eating occasions (per 2.6 eating occasions/24 hours;  $-1.1$ ;

**Table 1.** Baseline characteristics of the United States and the United Kingdom International Study on Macro/Micronutrients and Blood Pressure participants (n=2,385)

Variable	Men	Women	Total
n	1,232	1,153	2,385
	←————— <i>mean±standard deviation</i> —————→		
Age (y)	49.0±5.4	48.9±5.4	48.9±5.4
Education (y)	15.0±3.2	14.2±3.0****	14.6±3.1
Engagement in moderate and heavy physical activity (h/24 h)	3.3±3.2	2.8±2.8****	3.1±3.1
	←————— <i>n (%)</i> —————→		
Current smokers	230 (18.7)	176 (15.3)*	406 (17.0)
Any special diet	47 (3.8)	95 (8.2)****	142 (6.0)
Taking dietary supplements	539 (43.8)	641 (55.6)****	1,180 (49.5)
	←————— <i>mean±standard deviation</i> —————→		
Total energy intake (kcal/24 h)	2,692±625	1,963±415****	2,340±647
BMI <sup>a</sup>	28.6±4.7	28.1±6.3*	28.3±4.9
	←————— <i>n (%)</i> —————→		
Normal weight <sup>b</sup>	271 (22)	440 (38)****	711 (30)
Overweight <sup>c</sup>	579 (47)	363 (32)****	942 (39)
Obese <sup>d</sup>	382 (31)	350 (30)	732 (31)
	←————— <i>mean±standard deviation</i> —————→		
Eating occasions per 24 h	4.6±1.3	5.0±1.2****	4.8±1.3
Ratio of evening/morning energy intake	3.4±1.8	3.3±1.7	3.4±1.8
Dietary energy density (kcal/g)	1.9±0.4	1.8±0.4****	1.8±0.4
NRF9.3 <sup>e</sup>	29.0±12.7	32.9±15.2****	30.9±14.1

<sup>a</sup>BMI=body mass index; calculated as kg/m<sup>2</sup>.

<sup>b</sup>BMI<24.9.

<sup>c</sup>BMI 25.0 to <29.9.

<sup>d</sup>BMI≥30.0.

<sup>e</sup>NRF9.3=Nutrient Rich Food Index 9.3; calculated as the sum of the daily values of nutrients to encourage, subtracting the daily values for nutrients to limit based on 100 kcal: example; NRF9.3=(protein g/50 g+fiber g/25 g+vitamin A IU/5,000 IU+vitamin C mg/60 mg+vitamin E IU/30 IU+calcium mg/1,000 mg+iron mg/18 mg+magnesium mg/400 mg+potassium mg/3,500 mg—saturated fat g/20 g—added sugars g/50 g—sodium mg/2,400 mg)×100.

\*Significant at *P*<0.05.

\*\*\*\*Significant at *P*<0.0001.

95% CI –1.6 to –0.7) and with NRF9.3 (per 28.2; –1.7; 95% CI –2.2 to –1.1), and positively associated with dietary energy density (per 0.8 kcal/g; 1.8 kg/m<sup>2</sup>; 95% CI 1.4 to 2.3), after adjustment for sex, age, and population sample (Table 5). Association of BMI with ratio of evening/morning energy intake was also positive (per ratio of 3.6; 0; 95% CI 0.04 to 0.2). Results of sensitivity analyses (Table 6, available online at [www.andjrn.org](http://www.andjrn.org)) are comparable to our main findings, except for the association of BMI with ratio of evening/morning energy intake after excluding participants diagnosed with diabetes mellitus and/or cardiovascular disease.

## DISCUSSION

### Principal Findings of the Study

This study demonstrates that dietary behavior, exemplified by frequent eating, is associated with lower BMI, possibly driven

by lower dietary energy density and an improvement in nutrition quality. Participants with a diet of fewer eating occasions may have a lifestyle associated with eating out in the evening. This may be characterized by energy-dense foods with lower nutrient density (eg, deep fried foods), alcohol consumption, and less emphasis on low-energy-dense foods with high nutrient density (eg, fruit and vegetables).

A higher evening energy intake relative to morning energy intake was positively associated with BMI. In addition, when participants were classified jointly by frequency of intake and time of intake, BMI was lower in the high-eating-frequency group compared to the low-eating-frequency group for both low and high evening energy intake.

### Comparison with Other Studies

Increased frequency of eating occasions has been linked to improvements in glucose homeostasis in both cohort studies

**Table 2.** Variables by category of eating occasion per day, United States and United Kingdom International Collaborative Study of Macronutrients, Micronutrients, and Blood Pressure Participants (n=2,385)<sup>a</sup>

Variables	No. of Eating Occasions/24 h				P for trend <sup>b</sup>
	<4	≥4 to <5	≥5 to <6	≥6	
Participants	←—————n—————→				
	577	795	601	412	
Men	←—————%—————→				
	64	52	45	43	
	←—————adjusted mean (95% CI)—————→				
BMI <sup>cd</sup>	29.0 (28.8-29.50)	28.4 (28.0-28.5)	28.1 (27.7-28.4)	27.3 (26.8-27.8)	<0.0001
Ratio of evening/morning energy intake <sup>c</sup>	4.5 (3.8-6.2)	4.1 (3.8-5.5)	2.1 (1.5-3.7)	2.3 (1.0-3.7)	0.09
Dietary energy density (kcal/g)	2.1 (1.9-2.2)	1.8 (1.8-1.9)	1.7 (1.6-1.8)	1.5 (1.4-1.6)	<0.0001
Nutrient Rich Food Index 9.3 <sup>d</sup>	28.1 (27.0-29.2)	30.1 (29.3-31.0)	31.8 (30.8-32.8)	34.3 (33.0-35.5)	<0.0001
Total energy intake (kcal/24 h)	2,472 (2,444-2,544)	2,402 (2,331-2,413)	2,294 (2,288-2,359)	2,129 (2,102-2,189)	<0.0001
Food energy (kcal/24 h)	2,052 (2,046-2,135)	1,988 (1,951-2,024)	1,910 (1,878-1,941)	1,725 (1,687-1,764)	<0.0001
Beverage energy (kcal/24 h)	420 (401-440)	414 (398-430)	384 (365-403)	404 (381-427)	<0.0001
Alcohol (g/24 h) <sup>d</sup>	11.3 (10.1-12.6)	8.8 (7.8-9.8)	7.7 (6.5-8.8)	6.5 (5.1-7.9)	<0.0001
Food weight (g/24 h)	974 (948-1,001)	1,084 (1,062-1,105)	1,140 (1,115-1,165)	1,150 (1,120-1,222)	<0.0001
Beverage weight (g/24 h) <sup>e</sup>	1,701 (1,631-1,770)	1,594 (1,537-1,651)	1,574 (1,524-1,623)	1,562 (1,501-1,622)	0.02
Food groups (g/1,000 kcal)					
Whole-fat dairy	26.4 (22.5-30.2)	26.6 (23.1-30.1)	28.1 (24.3-31.9)	22.8 (18.4-27.2)	0.21
Low-fat/medium-fat dairy	69.9 (61.7-78.2)	83.3 (75.9-90.7)	93.7 (85.5-101.9)	108.2 (98.9-117.6)	<0.0001
Red meat	31.5 (29.4-33.6)	27.2 (25.4-29.1)	27.0 (25.0-29.1)	22.0 (19.6-24.3)	<0.0001
Fish	7.7 (6.5-8.9)	8.1 (7.0-9.2)	6.8 (5.6-8.0)	7.4 (6.1-8.8)	0.23
Raw vegetables	22.8 (20.9-24.2)	25.1 (26.0-29.2)	28.6 (26.5-29.9)	31.6 (29.2-33.5)	0.02
Cooked vegetables	41.6 (39.0-45.1)	45.1 (43.8-47.5)	50.0 (47.0-51.7)	56.7 (53.2-59.2)	0.02
Fruit	34.7 (29.2-40.3)	47.5 (42.5-52.5)	58.4 (52.9-63.9)	72.4 (66.1-78.7)	<0.0001
Cakes and pies	6.5 (5.4-7.4)	6.1 (5.7-7.1)	5.4 (4.5-6.1)	5.3 (4.2-5.4)	0.06

<sup>a</sup>Adjusted for sex, age, educational level, hours engaged in moderate and heavy physical activity, smoking, on a special diet, dietary supplement use, and population sample.

<sup>b</sup>A Bonferroni threshold of  $P < 0.003$  denoted statistical significance.

<sup>c</sup>BMI=body mass index; calculated as  $\text{kg}/\text{m}^2$ .

<sup>d</sup>Also adjusted for total energy intake (kcal/24 h).

<sup>e</sup>Drinking water excluded.

and clinical trials.<sup>29,30</sup> Data on eating frequency and body weight are inconsistent. In a recent longitudinal study of eating frequency and BMI in adolescent females based on two 3-day dietary records, less-frequent intake during the day was associated with greater BMI and waist circumference, consistent with our findings.<sup>9</sup>

Our finding that the ratio of evening/morning energy intake across eating occasion categories was higher in those having fewer eating occasions may be explained by having large boluses of food, with the larger portion of their diet consumed in the evening. Evidence from studies on shift work and health provide some insight into the association between behavioral changes (eg, diet, exercise) and overweight. Shift work is defined as work performed at a time other than regular daytime hours. The nurses and midwives cohort study found higher prevalence of overweight and

obesity among shift workers compared to day workers.<sup>31</sup> Shift workers have increased night-time intake compared to daytime, mainly from energy-dense foods,<sup>32,33</sup> and experience increased likelihood of weight gain.<sup>34</sup> This is comparable to our findings, where those eating less frequently and mostly in the evening showed higher consumption of alcohol, lower nutrient density, and lower fruit and vegetable intake. This provides an insight into the lifestyle and dietary behaviors associated with an obesogenic environment.

### Possible Mechanisms

The observed association between BMI, total energy intake, and frequency of eating occasions is likely to be multifactorial. It has been suggested in clinical feeding trials that reduced eating occasions per day may have a negative effect

**Table 4.** Comparison between groups of participants with extreme low and high eating occasions by ratio of evening/morning energy intake, United States and United Kingdom International Collaborative Study of Macronutrients, Micronutrients, and Blood Pressure participants (n=520)<sup>a</sup>

Variables	<4 Eating occasions/24 h and >1.8 ratio of evening/morning energy intake	≥6 Eating occasions/24 h and ≤1.8 ratio of evening/morning energy intake	P for t test <sup>b</sup>
	←-----n-----→		
Participants	317	203	
	←-----%-----→		
Men	68	41	
	←-----adjusted mean (95% CI)-----→		
Body mass index <sup>cd</sup>	29.2 (28.5-29.9)	27.3 (26.6-28.1)	0.01
Dietary energy density (kcal/g)	2.2 (2.1-2.3)	1.5 (1.4-1.6)	0.003
Nutrient Rich Food Index 9.3 <sup>d</sup>	27.5 (25.9-29.1)	34.8 (32.9-36.7)	<0.0001
Total energy intake (kcal/24 h)	2,548 (2,467-2,627)	2,189 (2,120-2,256)	<0.0001
Food energy (kcal/24 h)	2,125 (2,079-2,140)	1,804 (1,780-1,830)	<0.0001
Beverage energy (kcal/24 h)	423 (390.4-455.8)	385 (347-422)	0.22
Alcohol (g/24 h) <sup>d</sup>	12.0 (9.9-14.1)	6.4 (3.9-8.9)	<0.001
Food weight (g/24 h)	950 (916-984)	1,220 (1,172-1,269)	<0.0001
Beverage weight (g/24 h) <sup>e</sup>	2,513 (2,384-2641)	2,348 (2,219-2,476)	0.03
Food groups (g/1,000 kcal)			
Whole-fat dairy	27.8 (22.9-32.6)	23.6 (17.9-29.3)	0.31
Low-fat/fat-free dairy	62.6 (52.4-72.9)	108.9 (96.9-121.0)	<0.0001
Red meat	32.8 (30.1-35.5)	22.9 (19.6-26.1)	<0.0001
Fish	6.7 (5.6-7.8)	6.6 (5.0-8.1)	0.32
Raw vegetables	26.7 (23.5-30.0)	25.1 (21.3-28.9)	0.41
Cooked vegetables	40.6 (37.4-43.6)	55.8 (50.7-59.1)	0.05
Fruit	32.5 (25.6-39.4)	81.8 (73.7-89.9)	<0.0001
Cakes and pies	5.6 (4.2-7.0)	6.1 (4.4-7.7)	0.62

<sup>a</sup>Adjusted for sex, age, educational level, hours engaged in moderate and heavy physical activity, smoking, on a special diet, dietary supplement use, and population sample.

<sup>b</sup>A Bonferroni threshold of  $P < 0.003$  denoted statistical significance.

<sup>c</sup>Calculated as  $\text{kg}/\text{m}^2$ .

<sup>d</sup>Also adjusted for total energy intake (kcal/24 h).

<sup>e</sup>Drinking water excluded.

**Table 5.** Estimated mean body mass index differences per 2 standard deviations higher difference in eating occasions, ratio of evening/morning energy intake, dietary energy density, and Nutrient Rich Food Index 9.3 in the United States and the United Kingdom International Collaborative Study of Macronutrients, Micronutrients, and Blood Pressure participants (n=2,385)<sup>a</sup>

Variable	Body Mass Index		P value
	Difference	95% CI	
Eating occasions per 24 h <sup>b</sup> (2 SD <sup>c</sup> =2.6)	-1.1	-1.6 to -0.7	<0.0001
Ratio of evening/morning energy intake <sup>b</sup> (2 SD=3.6)	0.2	0.04 to 0.2	0.06
Dietary energy density (kcal/g) (2 SD=0.8)	1.8	1.4 to 2.3	<0.0001
Nutrient Rich Food Index 9.3 <sup>b</sup> (2 SD=28.2)	-1.7	-2.2 to -1.1	<0.0001

<sup>a</sup>Adjusted for sex, age, and population sample.

<sup>b</sup>Also adjusted for total energy intake (kcal/24 h).

<sup>c</sup>SD=standard deviation.

on appetite control.<sup>6,35</sup> There is evidence that a number of hormonal and nutritional signals can enhance appetite suppression with an increase in meal frequency.<sup>36</sup> This leads to a reduction in energy intake<sup>36</sup> and delayed gastric emptying, which therefore decreases the feeling of hunger.<sup>37</sup> Isocaloric increase in meal frequency in the morning may lead to a decrease in subjective feelings of hunger, possibly due to a complex interaction of anorectic signals from an increase in glucagon-like peptide 1 and a decrease in ghrelin.<sup>38</sup>

The participants' data demonstrate a clear association between eating frequency and dietary energy density as well as nutrient density. A recent systematic review of cohort studies and randomized controlled trials supports an inverse association between body weight and dietary energy density.<sup>39</sup> Having fewer meals per 24 hours with large amounts of energy-dense food consumed at each meal has been shown to promote overeating and is associated with high total energy intake, especially in overweight individuals.<sup>40</sup> Although the mechanism behind this relationship is not clear, a recent randomized clinical trial suggests that lower dietary energy density is related to a decrease in the hunger-stimulating hormone ghrelin, and an increase in peptide YY, a satiety hormone.<sup>14</sup>

The observed positive association between evening intake and BMI may be linked to a possible decline in insulin sensitivity during the evening, caused by elevation in nonessential fatty acids.<sup>41</sup> Our finding that those with lower evening/morning energy intake and more frequent eating occasions had lower BMI and higher nutrient density—while those eating less frequently and mostly in the evening showed higher consumption of alcohol, lower nutrient density, and lower fruit and vegetable intake—may provide an insight into lifestyle and dietary behaviors. There may be less access to fruits and vegetables during a later time frame or during an evening restaurant meal. This is a common pattern associated with eating out, where energy-dense food is mostly served, often consumed with alcohol, and most likely in the late evening.

### Strengths and Weakness of Our Study

The strengths of the INTERMAP study include the diverse population samples (eight samples in the United States and two samples in the United Kingdom), highly standardized multiple measures of dietary intake (four 24-hour dietary recalls), and extensive control for multiple dietary and other lifestyle factors (eg, cigarette smoking, education level, alcohol consumption) as potential confounders. The correlations between dietary and urinary variables in our study were higher than those previously reported from population-wide studies, mostly using food frequency questionnaires.<sup>42</sup>

Inconsistent findings in previous studies between eating frequency and body weight may be attributed to methodological issues; for example, under-reporting of energy, variations in definitions of eating occasions, and the validity and reliability of dietary assessment methods.<sup>5,43</sup> The present study addressed these limitations by use of multiple highly standardized 24-hour dietary recalls, exclusion from analyses of participants who potentially under-reported their energy intake, and exclusion of beverages from the eating occasion count to ensure that findings were not influenced by consumption of beverages.

Limitations of our study include its cross-sectional design, which does not allow for inference of causal relationships, possibility of regression dilution bias due to imprecise measures, and possible residual confounding. However, extensive measures were applied to minimize those limitations (repeated measurements, extensive observer training, standardized methods, open-end questions, and ongoing quality-control measures). It may also be that the mean eating occasion of 4 days may not be representative of long-term dietary habits, which are subject to seasonal/festival changes. Another possible limitation in estimating the independent association of eating frequency with BMI may be reverse causality, or due to other lifestyle factors that were not measured, for example, participants may skip meals in order to lose weight, or because of the demand of their jobs or stress, which can lead to comfort eating.

Although data collection for the INTERMAP study was conducted between 1996 and 1999, the mean caloric intake of Americans in 2009 to 2010 was 2,606 kcal/24 hours for men and 1,776 kcal/24 hours for women, comparable to that of INTERMAP participants (2,692 kcal/24 hours for men, 1,963 kcal/24 hours for women).<sup>44</sup>

To understand the implications of these findings on the public health management of obesity, there is need for additional research. A randomized controlled feeding trial, addressing all previous limitations, is suggested. The aim is to examine the impact of a low meal frequency that is high in energy density and a high meal frequency that is low in energy density on body weight.

### CONCLUSIONS

Our findings demonstrated that lower BMI levels in more frequent eaters are associated with consumption of lower dietary energy density and higher nutrient quality foods. Modifying eating behavior through more frequent meals of low dietary energy density and high nutrient quality may be an important approach to control epidemic obesity.

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**Table 3.** Variables by quartiles of ratio of evening/morning energy intake, United States and United Kingdom International Collaborative Study of Macronutrients, Micronutrients, and Blood Pressure participants (n=2,385)<sup>a</sup>

Variable	Ratio of Evening/Morning Energy Intake				P for trend <sup>b</sup>
	<1.0	≥1.0 to <1.5	≥1.5 to <2.0	≥2.0	
	←-----n-----→				
Participants	594	595	595	595	
	←-----%-----→				
Men	47	51	49	59	
	←-----adjusted mean (95% CI)-----→				
BMI <sup>c</sup>	27.5 (27.1-27.9)	27.9 (27.5-28.4)	28.1 (27.7-28.6)	28.7 (28.3-29.2)	0.08
Dietary energy density (kcal/g)	1.7 (1.7-1.8)	1.8 (1.8-1.9)	1.8 (1.8-1.9)	1.9 (1.9-2.0)	0.02
Nutrient Rich Food Index 9.3	31.6 (30.5-32.5)	31.6 (30.6-32.6)	31.5 (30.5-32.6)	28.5 (27.4-29.5)	<0.0001
Total energy (kcal/24 h)	2,199 (2,165-2,250)	2,325 (2,288-2,373)	2,332 (2,292-2,370)	2,360 (2,310-2,399)	0.04
Alcohol (g/24 h)	7.0 (5.8-8.2)	8.1 (6.9-9.3)	8.8 (7.7-10.0)	11.0 (10.0-12.1)	<0.0001

<sup>a</sup>Adjusted for sex, age, educational level, hours engaged in moderate and heavy physical activity, smoking, on a special diet, dietary supplement use, (total energy intake, kcal/24 h), and population sample.

<sup>b</sup>A Bonferroni threshold of  $P < 0.01$  denoted statistical significance.

<sup>c</sup>BMI=body mass index; calculated as kg/m<sup>2</sup>.

**Table 6.** Estimated mean body mass index differences per 2 standard deviations higher difference in eating occasions, ratio of evening/morning energy intake, dietary energy density, and Nutrient Rich Food Index Score 9.3 in subcohorts, United States and United Kingdom International Collaborative Study of Macronutrients, Micronutrients, and Blood Pressure participants

Variable	Body Mass Index			P value
	No. of participants	Difference	95% CI	
<b>Excluding participants on weight loss diet<sup>a</sup></b>	2,243			
Eating occasions per 24 h <sup>bc</sup> (2 SD=2.6)		-1.2	-1.6 to -0.7	<0.0001
Ratio of evening/morning energy intake <sup>bc</sup> (2 SD=3.6)		0.04	0.01 to 0.1	0.07
Dietary energy density (kcal/g) <sup>b</sup> (2 SD=0.8)		1.9	1.4 to 2.4	<0.0001
Nutrient Rich Food Index 9.3 <sup>bc</sup> (2 SD=28.2)		-1.6	-2.0 to -1.1	<0.0001
<b>Excluding participants with DM<sup>e</sup>/CVD<sup>fg</sup></b>	2,054			
Eating occasions per 24 h <sup>bc</sup> (2 SD=2.6)		-0.8	-1.3 to -0.4	0.0008
Ratio of evening/morning energy intake <sup>bc</sup> (2 SD=3.6)		0.04	-0.03 to 0.1	0.8
Dietary energy density (kcal/g) <sup>b</sup> (2 SD=0.8)		1.8	1.4 to 2.3	<0.0001
Nutrient Rich Food Index 9.3 <sup>bc</sup> (2 SD=28.2)		-1.4	-1.8 to -0.9	<0.0001

<sup>a</sup>Participants reporting after a weight-loss diet were excluded.

<sup>b</sup>Adjusted for sex, age, and population sample.

<sup>c</sup>Also adjusted for total energy intake (kcal/24 h).

<sup>d</sup>SD=standard deviation.

<sup>e</sup>DM=diabetes mellitus.

<sup>f</sup>CVD=cardiovascular disease.

<sup>g</sup>Participants diagnosed with diabetes mellitus or cardiovascular diseases were excluded.