Original Article

# Low riboflavin intake is associated with cardiometabolic risks in Korean women

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**Background and Objectives:** Metabolic syndrome is a leading global public health concern. Nutritional approaches are important for preventing and managing cardiometabolic risks, including metabolic syndrome. The aim of this study was to examine the potential association between riboflavin intake and cardiometabolic risks according to sex among Koreans. **Methods and Study Design:** We used data from the Korea National Health and Nutrition Examination Survey 2015–2016, a nationwide cross-sectional survey that assesses the health and nutritional status of the Korean population. A total of 6,062 individuals aged ≥19 years were included. The nutrition survey was performed using 24-h dietary recall. **Results:** A significant association was observed between low riboflavin intake with only increased HDL-cholesterol (OR 1.362, 95% CI 1.017-1.824, $p$=0.038) among metabolic syndrome and its components in men, whereas insufficient riboflavin intake was positively associated with hypertension (OR 1.352, 95% CI 1.085-1.685, $p$=0.007), diabetes (OR 1.493, 95% CI 1.137-1.959, $p$=0.004) and metabolic syndrome (OR 1.289, 95% CI 1.014-1.640, $p$=0.038) in women after adjusting for the other covariates. For post-menopausal women, central obesity was also correlated with insufficient riboflavin intake (OR 1.315, 95% CI 1.019-1.696, $p$=0.035). **Conclusions:** Insufficient riboflavin intake may contribute to development of cardiometabolic disorder, particularly in women. It was also found that riboflavin may have different influences on its risks in women according to menopausal status. This study highlighted the importance of public policies targeted at these sex-specific groups for reducing cardiometabolic risks.

**Key Words: riboflavin, vitamin B-2, metabolic syndrome, cardiometabolic risk, women**

## INTRODUCTION

Cardiometabolic disorders, such as CVD and type 2 diabetes, are currently the leading causes of mortality and public health concerns worldwide.[1] Metabolic syndrome (MetS) is a cluster of conditions, including central obesity, high blood sugar, high blood pressure (BP), high serum triglycerides (TGs) and low serum HDL-cholesterol, and refers to a core of cardiometabolic risks.[2,3] It was estimated that one in three adults had MetS in the United States.[4] Similarly, the prevalence of MetS reached 22.4% among Korean adults in 2015.[5] Although its cause remains unclear, MetS may be attributable to an underlying disorder of energy storage and utilisation, followed by oxidative injury. To this end, nutritional approaches are important for preventing or managing the syndrome.

Riboflavin, also known as vitamin B-2, is a water-soluble vitamin found in a variety of foods including dairy products, meat, fish, and green vegetables.[6] It is essential for haematological, neurological, cardiovascular, and endocrine system functioning by aiding normal tissue respiration via redox reactions and energy metabolism, with flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN) as biologically active forms.[6] A recent national nutrition survey in Korea reported poor average riboflavin intake below the Estimated Average Requirement (EAR) for approximately half of Korean people (41.7% in 2016).[7]

Despite the importance and insufficient intake of riboflavin, studies regarding how riboflavin might reduce cardiometabolic risk are limited. Further, to the best of our knowledge, there has been no study on sex-based differences in the association of riboflavin intake with MetS that used a large, nationwide sample. Therefore, the aim of this study was to examine the association between riboflavin intake and cardiometabolic risks (such as MetS) according to sex-based differences among Korean adults from 2015 to 2016.

## METHODS

### *Data source and study population*

The Korea National Health and Nutrition Examination Survey (KNHANES) is a nationwide cross-sectional survey that assesses the health and nutritional status of a representative Korean population. The survey was per-

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formed by the Korea Centers for Disease Control and Prevention.[8] This study was based on data obtained from KNHANES 2015–2016. Participants were adults, aged 19 years or older, who participated in at least one health interview, physical examination, laboratory measure, or nutrition survey. Participants who were aged 18 years or younger, pregnant or lactating were excluded due to potential unexpected metabolic effects and nutritional requirements or other covariates. Current smokers were also excluded considering the obvious sex-specific differences in the rate of current smoking among Korean adults (40.7% for men and 6.4% for women in 2016) and the strong evidence as an important risk factor for CVD.[7,9] For the KNHANES, informed consent was obtained from all participants. The institutional review board of the Korea Centers for Disease Control and Prevention approved the KNHANES (2015-01-02-6C).

***Demographic and health-related covariates***

Information on participants' demographics, including age, sex, health-related behaviours (e.g. cigarette smoking, alcohol use and physical activity), menopausal status, use of oral contraceptives and diagnosed medical conditions, was gathered through face-to-face interviews or self-report. Participants who smoked ≥100 cigarettes in their lifetime and who reported smoking currently were regarded as 'current' smokers. Participants were considered alcohol 'users' if they consumed seven or more drinks for men, and five or more drinks for women, at least twice a week. The 'regular' physical activity group consisted of those who engaged in moderate activities for ≥30 min in a day, at least 5 d a week, or in vigorous activities for ≥20 min in a day, at least 3 d a week.[10] Participants were also asked if they had chronic health conditions, including hypertension, diabetes, or dyslipidaemia that had been diagnosed by a health professional. The information on chronic conditions was also based on self-reported medical history.

***Clinical and laboratory measurements***

The health examination collected information regarding anthropometry, BP and blood analysis. According to standardised protocols, all health examinations were conducted by trained medical personnel and all pieces of equipment were calibrated regularly. BMI was calculated by dividing weight in kilograms by the square of height in metres, using data obtained wearing minimal clothing. Waist circumference (WC) was measured at the midpoint of the interval between the lower part of rib and the upper part of the iliac crest. BP was measured on each participant's right arm while seated and after a 5 min rest using a standard sphygmomanometer [Wall Unit 33(0850), Baumanometer ®, NY, US]. Venous blood samples were obtained for measurement of blood glucose and lipid profile after fasting for 12 h.

***Nutrition assessment***

A nutrition survey was conducted using a 24-h dietary recall by professional interviewers consisted of nurses, a dietitian, and health science graduates. Daily intake of energy and nutrients was further calculated from consumed foods or dietary supplements that were reported.

***Definition of MetS***

MetS was defined according to the US National Cholesterol Education Programme's Adult Treatment Panel III (NCEP/ATP III) criteria, adapted for Asians.[11] MetS was diagnosed as the presence of at least three of the following five criteria: (1) central obesity (WC ≥90 cm for men or ≥85 cm for women); (2) HDL-cholesterol <40 mg/dL for men, <50 mg/dL for women; (3) serum TGs ≥150 mg/dL; (4) increased BP (systolic ≥130 mmHg, diastolic ≥85 mmHg, or under treatment of hypertension); (5) fasting blood glucose (FBG) ≥100 mg/dL or under treatment for diabetes.

***Statistical analysis***

Statistical analyses were conducted using the SPSS, version 23 (SPSS Inc., Chicago, IL, USA). All analyses used sample weights assigned to participants to represent the Korean population, which were considered using estimated response probability and post-stratification. The participants were categorised into two groups according to riboflavin intake or the presence of MetS, to identify and compare between-group characteristics of the participants. Riboflavin intake was classified by adherence to the Recommended Nutrient Intake (RNI): 1.5 mg/d for men and 1.2 mg/d for women, according to DRIs for Koreans (KDRI).[12] Categorical variables were expressed as frequencies and weighted percentages of participants using Rao-Scott adjusted chi-squared tests, while continuous variables were expressed as means with their standard errors using ANOVA. Multivariate binary logistic regression was used to estimate the association between riboflavin intake and MetS, adjusting for age, alcohol use, physical activity, oral contraceptive use, menopause, and each riboflavin intake from the 4 most used food sources including cereals, vegetables, meats, and eggs, and supplementary sources. Use of oral contraceptives was subjected to multivariate modelling to control for residual confounding, considering the interaction between oral contraceptives and riboflavin, as suggested by Newman et al.[13] Adjusted ORs and 95 % CI for MetS and other cardiometabolic risks were calculated according to adherence to the RNI of riboflavin. $p$ values of <0.05 were considered statistically significant.

## RESULTS

A total of 20,311 (9,505 in 2015 and 10,806 in 2016) Korean men and women were selected using a two-stage stratified cluster and complex sampling method in the KNHANES 2015-2016. Of these, 15,530 (7,380 in 2015 and 8,150 in 2016) participants who participated in one or more health interviews, health examinations, or nutrition surveys were included. Finally, a total of 6,062 (2,023 for men and 4,039 for women) individuals were included in the statistical analysis after participants who were aged <19 years old, pregnant, lactating, current smoking or who had missing data were excluded.

***Characteristics of participants according to riboflavin intake***

The mean intake of riboflavin at baseline was 1.61±0.03 mg/d in men and 1.21±0.01 mg/d in women (Table 1). Overall, 58.8% (53% men and 57.2% women) of the par-

**Table 1.** General characteristics of men and women, according to riboflavin intakes

| Variables† | Men | | Total | *p* value‡ | Women | | Total | *p* value |
|---|---|---|---|---|---|---|---|---|
| | Riboflavin intake (mg/day) | | | | Riboflavin intake (mg/day) | | | |
| | <1.5 | ≥1.5 | | | <1.2 | ≥1.2 | | |
| Total | 1174 (53.0) | 849 (47.0) | 2023 (100.0) | | 2388 (57.2) | 1651 (42.8) | 4039 (100.0) | |
| Age (years) | | | | <0.001 | | | | <0.001 |
| 19-29 | 121 (19.5) | 105 (18.6) | 226 (19.1) | | 209 (14.3) | 184 (17.5) | 393 (15.7) | |
| 30-39 | 84 (11.4) | 122 (19.9) | 206 (15.4) | | 320 (14.5) | 291 (18.5) | 611 (16.2) | |
| 40-49 | 131 (16.4) | 158 (21.6) | 289 (18.8) | | 386 (18.6) | 374 (23.2) | 760 (20.6) | |
| 50-59 | 168 (17.8) | 169 (21.6) | 337 (19.5) | | 436 (19.8) | 384 (22.4) | 820 (21.0) | |
| 60-69 | 291 (15.4) | 180 (11.3) | 471 (13.5) | | 481 (15.1) | 273 (12.4) | 754 (13.9) | |
| ≥70 | 379 (19.5) | 115 (7.1) | 494 (13.7) | | 556 (17.7) | 145 (5.9) | 701 (12.7) | |
| Alcohol use | | | | 0.322 | | | | 0.016 |
| Yes | 118 (11.3) | 119 (12.9) | 237 (12.1) | | 65 (2.8) | 65 (4.5) | 130 (3.5) | |
| No | 1056 (88.7) | 730 (87.1) | 1786 (87.9) | | 2323 (97.2) | 1586 (95.5) | 3909 (96.5) | |
| Regular physical activity | | | | <0.001 | | | | <0.001 |
| Yes | 533 (52.4) | 509 (63.5) | 1042 (57.6) | | 975 (45.0) | 786 (51.2) | 1761 (47.7) | |
| No | 641 (47.6) | 340 (36.5) | 981 (42.4) | | 1413 (55.0) | 865 (48.8) | 2278 (52.3) | |
| Oral contraceptive use | | | | | | | | 0.013 |
| Yes | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 492 (18.8) | 272 (15.4) | 764 (17.4) | |
| No | 1174 (100.0) | 849 (100.0) | 2023 (100.0) | | 1896 (81.2) | 1379 (84.6) | 3275 (82.6) | |
| Menopause | | | | | | | | <0.001 |
| Yes | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 1429 (50.6) | 765 (38.7) | 2194 (45.5) | |
| No | 1174 (100.0) | 849 (100.0) | 2023 (100.0) | | 959 (49.4) | 886 (61.3) | 1845 (54.5) | |
| Hypertension | | | | 0.002 | | | | <0.001 |
| Yes | 507 (34.8) | 299 (27.5) | 806 (31.4) | | 876 (29.9) | 360 (17.7) | 1236 (24.7) | |
| No | 667 (65.2) | 550 (72.5) | 1217 (68.6) | | 1512 (70.1) | 1291 (82.3) | 2803 (75.3) | |
| Diabetic mellitus | | | | <0.001 | | | | <0.001 |
| Yes | 213 (13.4) | 99 (7.9) | 312 (10.8) | | 327 (11.6) | 120 (5.8) | 447 (9.1) | |
| No | 961 (86.6) | 750 (92.1) | 1711 (89.2) | | 2061 (88.4) | 1531 (94.2) | 3592 (90.9) | |
| Dyslipidemia | | | | 0.319 | | | | <0.001 |
| Yes | 408 (33.9) | 285 (31.4) | 693 (32.7) | | 827 (31.4) | 472 (25.0) | 1299 (28.7) | |
| No | 766 (66.1) | 564 (68.6) | 1330 (67.3) | | 1561 (68.6) | 1179 (75.0) | 2740 (71.3) | |
| Metabolic syndrome | | | | 0.169 | | | | <0.001 |
| Yes | 394 (30.0) | 260 (26.8) | 654 (28.5) | | 764 (27.4) | 359 (18.2) | 1123 (23.5) | |
| No | 780 (70.0) | 589 (73.2) | 1369 (71.5) | | 1624 (72.6) | 1292 (81.8) | 2916 (76.5) | |
| Central obesity | | | | 0.048 | | | | <0.001 |
| Yes | 359 (29.2) | 300 (33.9) | 659 (31.4) | | 797 (29.6) | 424 (22.6) | 1221 (26.6) | |
| No | 815 (70.8) | 549 (66.1) | 1364 (68.6) | | 1591 (70.4) | 1227 (77.4) | 2818 (73.4) | |
| Blood pressure (mmHg): systolic ≥130 or diastolic ≥85 or medication for hypertension | | | | 0.002 | | | | <0.001 |
| Yes | 646 (47.8) | 397 (40.1) | 1043 (44.2) | | 1048 (36.6) | 489 (25.0) | 1537 (31.6) | |
| No | 528 (52.2) | 452 (59.9) | 980 (55.8) | | 1340 (63.4) | 1162 (75.0) | 2502 (68.4) | |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
†Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
‡*p* values are from Rao-scott $\chi^2$ test or ANOVA.

**Table 1.** General characteristics of men and women, according to riboflavin intakes (cont.)

| Variables† | Men | | Total | *p* value‡ | Women | | Total | *p* value |
|---|---|---|---|---|---|---|---|---|
| | Riboflavin intake (mg/day) | | | | Riboflavin intake (mg/day) | | | |
| | <1.5 | ≥1.5 | | | <1.2 | ≥1.2 | | |
| Fasting blood glucose (mg/dL): ≥100 or medication for diabetes | | | | 0.284 | | | | <0.001 |
| Yes | 543 (38.4) | 359 (35.7) | 902 (37.1) | | 812 (30.7) | 420 (22.0) | 1232 (27.0) | |
| No | 631 (61.6) | 490 (64.3) | 1121 (62.9) | | 1576 (69.3) | 1231 (78.0) | 2807 (73.0) | |
| Triglycerides (mg/dL) ≥150 | | | | 0.352 | | | | 0.007 |
| Yes | 403 (35.0) | 283 (32.6) | 686 (33.9) | | 582 (21.6) | 326 (17.8) | 908 (20.0) | |
| No | 771 (65.0) | 566 (67.4) | 1337 (66.1) | | 1806 (78.4) | 1325 (82.2) | 3131 (80.0) | |
| HDL-cholesterol (mg/dL): men <40, women <50 | | | | 0.004 | | | | 0.003 |
| Yes | 331 (26.5) | 185 (19.7) | 516 (23.3) | | 1029 (39.5) | 628 (34.4) | 1657 (37.3) | |
| No | 843 (73.5) | 664 (80.3) | 1507 (76.7) | | 1359 (60.5) | 1023 (65.6) | 2382 (62.7) | |
| BMI (kg/m²) | 24.4±0.13 | 24.9±0.14 | 24.6±0.10 | 0.003 | 23.5±0.10 | 23.2±0.10 | 23.4±0.07 | 0.019 |
| Waist circumference (cm) | 86.1±0.34 | 86.7±0.35 | 86.4±0.25 | 0.160 | 79.7±0.29 | 78.2±0.29 | 79.1±0.23 | <0.001 |
| Systolic blood pressure (mmHg) | 121±0.49 | 119±0.55 | 120±0.38 | 0.005 | 117±0.43 | 113±0.41 | 115±0.33 | <0.001 |
| Diastolic blood pressure (mmHg) | 77.2±0.34 | 78.3±0.36 | 77.7±0.26 | 0.023 | 73.3±0.24 | 73.0±0.28 | 73.1±0.19 | 0.402 |
| Fasting blood glucose (mg/dL) | 103±0.99 | 99.7±0.80 | 101.2±0.69 | 0.015 | 98.4±0.55 | 95.4±0.51 | 97.1±0.41 | <0.001 |
| Total cholesterol (mg/dL) | 189±1.36 | 191±1.56 | 190±1.05 | 0.187 | 192±0.87 | 194±1.08 | 193±0.69 | 0.180 |
| Triglycerides (mg/dL) | 148±4.27 | 147±5.71 | 148±3.55 | 0.967 | 115±1.75 | 108±2.13 | 112±1.46 | 0.005 |
| LDL-cholesterol (mg/dL) | 113±1.23 | 114±1.33 | 113±0.94 | 0.320 | 115±0.76 | 116±0.95 | 116±0.62 | 0.346 |
| HDL-cholesterol (mg/dL) | 47.4±0.41 | 48.5±0.43 | 47.9±0.28 | 0.078 | 54.1±0.32 | 56.1±0.39 | 55.0±0.26 | <0.001 |
| Total energy intake (kcal/day) | 1875±21.6 | 2989±43.2 | 2399±29.2 | <0.001 | 1387±12.43 | 2158±20.4 | 1717±13.6 | <0.001 |
| Carbohydrates intake (g/day) | 301±3.43 | 406±5.62 | 350±3.73 | <0.001 | 236±2.42 | 323±3.42 | 273±2.30 | <0.001 |
| Protein intake (g/day) | 60.1±0.83 | 117±3.10 | 87.0±1.74 | <0.001 | 44.1±0.47 | 81.4±0.97 | 60.1±0.64 | <0.001 |
| Fat intake (g/day) | 35.6±0.90 | 79.1±2.21 | 56.0±1.39 | <0.001 | 26.6±0.49 | 55.2±0.94 | 38.8±0.57 | <0.001 |
| SFA intake (g/day) | 10.0±0.28 | 23.0±0.70 | 16.1±0.42 | <0.001 | 7.51±0.16 | 15.7±0.30 | 11.0±0.17 | <0.001 |
| MUFA intake (g/day) | 11.3±0.36 | 25.8±0.80 | 18.1±0.50 | <0.001 | 8.14±0.17 | 17.7±0.33 | 12.2±0.20 | <0.001 |
| PUFA intake (g/day) | 9.08±0.25 | 19.4±0.70 | 13.9±0.40 | <0.001 | 6.82±0.13 | 13.7±0.30 | 9.74±0.17 | <0.001 |
| Dietary fiber intake (g/day) | 21.5±0.38 | 32.7±0.59 | 26.8±0.40 | <0.001 | 17.4±0.22 | 28.1±0.45 | 22.0±0.26 | <0.001 |
| Total riboflavin intake (mg/day) | 0.98±0.01 | 2.33±0.04 | 1.61±0.03 | <0.001 | 0.75±0.01 | 1.81±0.02 | 1.21±0.01 | <0.001 |
| Riboflavin intake from cereals and grains | 0.18±0.01 | 0.37±0.02 | 0.27±0.01 | <0.001 | 0.14±0.00 | 0.26±0.01 | 0.18±0.00 | <0.001 |
| Riboflavin intake from meats | 0.12±0.01 | 0.36±0.02 | 0.23±0.01 | <0.001 | 0.08±0.00 | 0.23±0.01 | 0.15±0.00 | <0.001 |
| Riboflavin intake from vegetables | 0.18±0.00 | 0.32±0.01 | 0.24±0.01 | <0.001 | 0.13±0.00 | 0.27±0.01 | 0.19±0.00 | <0.001 |
| Riboflavin intake from eggs | 0.11±0.01 | 0.35±0.02 | 0.21±0.01 | <0.001 | 0.08±0.00 | 0.35±0.01 | 0.20±0.01 | <0.001 |
| Riboflavin intake from fruits | 0.04±0.00 | 0.07±0.00 | 0.06±0.00 | <0.001 | 0.05±0.00 | 0.08±0.00 | 0.06±0.00 | <0.001 |
| Riboflavin intake from milks and dairy products | 0.06±0.00 | 0.18±0.01 | 0.11±0.01 | <0.001 | 0.06±0.00 | 0.16±0.01 | 0.10±0.00 | <0.001 |
| Riboflavin intake from supplements | 0.29±0.00 | 0.70±0.05 | 0.48±0.02 | 0.222 | 0.21±0.00 | 0.46±0.02 | 0.32±0.00 | 0.313 |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
†Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
‡*p* values are from Rao-scott $\chi^2$ test or ANOVA.

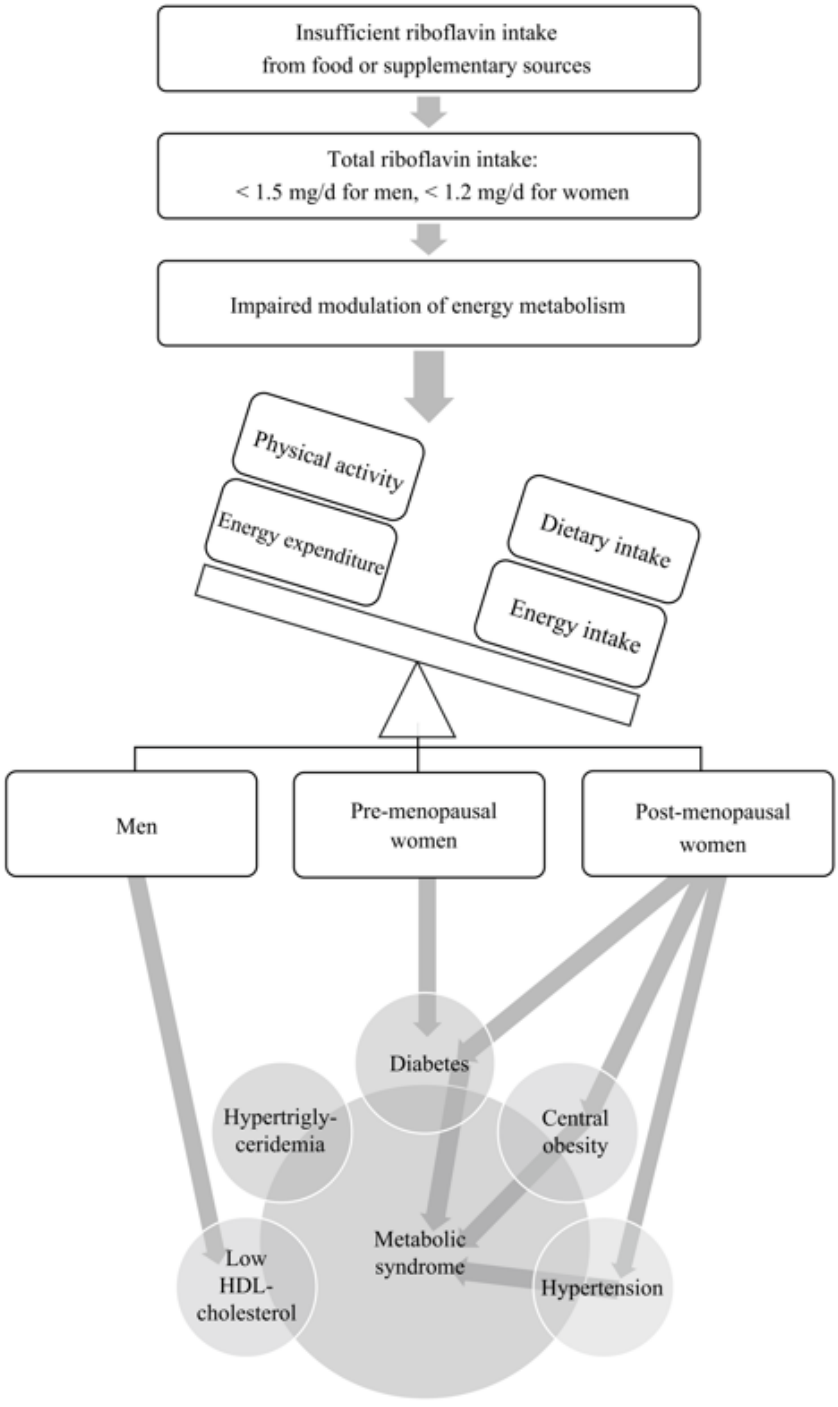


**Figure 1.** A schematic diagram that presents the pathways from insufficient riboflavin intake with food or supplementary sources to the development of cardiometabolic risks, including metabolic syndrome, via impaired modulation of energy metabolism along with other personal behaviours such as physical activity as energy expenditure.

ticipants had daily riboflavin intake below the RNI for Koreans. Sociodemographic and cardiometabolic characteristics, relative to riboflavin intake at baseline, are shown in Table 1. There were significant between-group differences in mean riboflavin intake when we compared intakes that were below and above the RNI for riboflavin, in both sexes (0.98±0.01 vs 2.33±0.04 mg/d, $p$<0.001 for men and 0.75±0.01 vs 1.81±0.02 mg/d, $p$<0.001 for women).

***Characteristics of participants with and without MetS***

Among the 6,062 participants at baseline, there were 654 (28.5%) men and 1,123 (23.5%) women with MetS and their general characteristics are listed in Supplementary Tables 1 and 2. Among men, those aged 50-59 years had the highest prevalence of MetS, whereas the prevalence of MetS increased with age in women ($p$<0.001). Unlike non-MetS women, women with MetS were more likely to be post-menopausal (76.8% vs 23.2%, $p$<0.001). The rate of participants with MetS was higher among post-menopausal women than pre-menopausal women (39.6% vs 10%, $p$<0.001). As shown in Supplementary Table 2, while half of post-menopausal women had hypertension, the prevalence of hypertension in pre-menopausal women was only 6.7% in the present study. Mean daily riboflavin intake was significantly lower in the MetS than in the

non-MetS group for both men (1.53±0.05 vs 1.65±0.04, $p$=0.038) and women (1.05±0.02 vs 1.25±0.02, $p$<0.001).

***Association of riboflavin intake with MetS and related conditions in men and women***

Table 2 presents the estimated OR and 95 % CI of MetS and related chronic conditions, by daily riboflavin intake, in men and women. Here, we used binary logistic regression analysis, adjusting for other covariates. ORs were estimated by comparing the prevalence of each chronic condition, by daily riboflavin intake, using the RNI for riboflavin as a reference. In men, we found no significant relationship between poor riboflavin intake and the prevalence of MetS or other related chronic conditions, except low HDL-cholesterol (OR 1.362, 95% CI 1.017-1.824, $p$=0.038), after adjusting for covariates (Table 2). On the other hand, there was significant inverse association between riboflavin intake and hypertension (OR 1.352, 95% CI 1.085-1.685, $p$=0.007) and between riboflavin intake and diabetes (OR 1.493, 95% CI 1.137-1.959, $p$=0.004) after adjusting for covariates in women. We also found that insufficient riboflavin intake was significantly correlated with the prevalence of MetS (OR 1.289, 95% CI 1.014-1.640, $p$=0.038) after adjusting for covariates in women.

***Association of riboflavin intake with MetS and related chronic conditions in pre- and post-menopausal women***

There were significantly more post-menopausal women in the MetS group than in the non-MetS group (Supplementary Table 1). We therefore evaluated the association of riboflavin intake and individual components of MetS, according to menopausal status, in women (Table 3). Table 3 further shows the ORs of individual components of MetS and related chronic diseases, by riboflavin intake, in pre- and post-menopausal women. There was no significant relationship between riboflavin intake and BP in pre-menopausal women ($p$>0.05), whereas insufficient riboflavin intake was positively associated with hypertension (OR 1.479, 95% CI 1.158-1.889, $p$=0.002) in post-menopausal women after adjusting for covariates. Riboflavin intake was inversely associated with diabetes in both pre- (OR 1.664, 95% CI 1.070-2.589, $p$=0.024) and post-menopausal women (OR 1.426, 95% CI 1.052-1.932, $p$=0.022). We found no significant association between riboflavin intake and central obesity in pre-menopausal women ($p$=0.956). However, among post-menopausal women with insufficient riboflavin intake, there was a positive correlation with central obesity after adjusting for other covariates (OR 1.315, 95% CI 1.019-1.696, $p$=0.035). There was also a significant association of poor riboflavin intake with the prevalence of MetS only in post-menopausal women (OR 1.304, 95% CI 1.005-1.692, $p$=0.045).

## DISCUSSION

Among Korean adults, insufficient riboflavin intake appears common, with 58.8% of participants exhibiting daily riboflavin intake below the RNI. This result is similar to the findings from a previous national nutrition survey in Korea that reported poor riboflavin intake (below EAR) among half of Koreans.[7] The prevalence of MetS was 28.5% in men and 23.5% in women. Among men, those aged 50-59 years had the highest prevalence of MetS, whereas in women, the prevalence of MetS increased with age. There were significantly more post-menopausal women in the MetS group than in the non-MetS group. Our findings are consistent with those of a previous report regarding the differences in prevalence of MetS by sex and age.[5] In men, no significant relationship between poor riboflavin intake and the prevalence of MetS or any other related chronic condition was found, except low HDL-cholesterol, after adjusting for covariates. On the other hand, there was a significant and positive association of insufficient riboflavin intake with the prevalence of hypertension, diabetes and also MetS after adjusting for covariates in women. This finding suggests that riboflavin deficiency contributes to the development of cardiometabolic risks, particularly in women. Additionally, riboflavin intake may exert disproportional effects on post-menopausal women compared with their pre-menopausal counterparts (Figure 1).

Evidenced managements of MetS include improving a wide range of personal behaviours, such as maintaining a healthy body weight, engaging in regular physical activity and consuming a healthy diet. Although, there has been no agreed pathophysiology for MetS or other cardiometabolic disorders, the effect of obesity, considering only BMI, on CVD is varied and affected by other cardiometabolic status.[14] Wahlqvist et al suggested a unified explanatory core mechanism of this syndrome, impaired energy regulation, which was found similarly in different ethnic groups.[15] They proposed disordered energy metabolism with its energy intake and expenditure as a consistent basis of MetS. Furthermore, Kiran et al have found that obesity-related inflammation released pro-inflammatory cytokines from adipose tissue, potentially contributing to the development of numerous cardiometabolic disorders.[16] Riboflavin reportedly plays a role in the regulation of cellular fuel metabolism and mitochondrial energy function,[6] but inflammation-related biomarkers were not analyzed in the present study. Particularly, we also found a significant relationship between poor riboflavin intake and central obesity among post-menopausal women. On the other hand, nutritional studies have found that high intake of foods rich in antioxidants, such as fruit and vegetables, whole grains, and MUFAs and PUFAs, was inversely associated with the development of MetS.[17,18] Antioxidants, including some specific micronutrients, have received worldwide attention since oxidative stress has an important role in the pathogenesis of obesity-related metabolic disorders.[19,20] Avignon et al and Whayne et al have shown that higher dietary or supplementary intake of antioxidants (such as vitamins A, C and E, folic acid, niacin, selenium and zinc) was associated with a reduced cardiometabolic risk.[20,21] Other studies produced mixed results regarding the ties between antioxidant intake and cardiometabolic risk.[19,22] Previous studies conducted in animal models indicated that riboflavin exert a direct or indirect protective effect against oxidative stress by converting or metabolising other antioxidants, including other vitamins and glutathione.[23,24] Similarly, this study showed that sufficient riboflavin intake might help reduce cardiometabolic risks by managing inflam-

**Table 2.** ORs (95% CI) of variables according to riboflavin intake after adjusting for covariates in men and women

| | | Men | | | Women | | |
|---|---|---|---|---|---|---|---|
| | | Riboflavin intake (mg/day) | | | Riboflavin intake (mg/day) | | |
| | | ≥1.5 | <1.5 | | ≥1.2 | <1.2 | |
| Variables | Model | OR | OR (95% CI) | *p* value | OR | OR (95% CI) | *p* value |
| Hypertension | 1† | 1 | 1.09 (0.85-1.41) | 0.506 | 1 | 1.39 (1.15-1.68) | <0.001 |
| | 2‡ | 1 | 1.06 (0.80-1.40) | 0.682 | 1 | 1.35 (1.09-1.69) | 0.007 |
| Diabetic mellitus | 1 | 1 | 1.44 (1.01-2.06) | 0.045 | 1 | 1.53 (1.18-1.97) | 0.001 |
| | 2 | 1 | 1.35 (0.94-1.93) | 0.104 | 1 | 1.49 (1.14-1.96) | 0.004 |
| Dyslipidemia | 1 | 1 | 1.17 (0.92-1.48) | 0.200 | 1 | 1.14 (0.97-1.34) | 0.111 |
| | 2 | 1 | 1.26 (0.98-1.63) | 0.078 | 1 | 1.12 (0.94-1.34) | 0.213 |
| Central obesity | 1 | 1 | 0.78 (0.62-0.98) | 0.032 | 1 | 1.15 (0.97-1.37) | 0.108 |
| | 2 | 1 | 0.80 (0.62-1.04) | 0.092 | 1 | 1.12 (0.93-1.36) | 0.224 |
| Blood pressure (mmHg): systolic ≥130 or diastolic ≥85 or medication for hypertension | 1 | 1 | 1.12 (0.89-1.41) | 0.338 | 1 | 1.22 (1.02-1.46) | 0.027 |
| | 2 | 1 | 1.08 (0.82-1.40) | 0.592 | 1 | 1.24 (1.02-1.50) | 0.030 |
| Fasting blood glucose (mg/dL): ≥100 or medication for diabetes | 1 | 1 | 0.97 (0.77-1.22) | 0.793 | 1 | 1.28 (1.08-1.53) | 0.006 |
| | 2 | 1 | 0.95 (0.73-1.24) | 0.692 | 1 | 1.27 (1.05-1.53) | 0.014 |
| Triglycerides (mg/dL) ≥150 | 1 | 1 | 1.18 (0.94-1.47) | 0.152 | 1 | 1.11 (0.93-1.34) | 0.255 |
| | 2 | 1 | 1.23 (0.96-1.57) | 0.102 | 1 | 1.05 (0.86-1.28) | 0.640 |
| HDL-cholesterol (mg/dL): men <40, women <50 | 1 | 1 | 1.39 (1.06-1.81) | 0.016 | 1 | 1.11 (0.95-1.29) | 0.188 |
| | 2 | 1 | 1.36 (1.02-1.82) | 0.038 | 1 | 1.08 (0.92-1.27) | 0.363 |
| Metabolic syndrome | 1 | 1 | 1.06 (0.83-1.36) | 0.620 | 1 | 1.28 (1.06-1.55) | 0.011 |
| | 2 | 1 | 1.12 (0.86-1.46) | 0.410 | 1 | 1.29 (1.01-1.64) | 0.038 |

HDL: high-density lipoprotein.
†Model 1: adjusted for age.
‡Model 2: adjusted for age, alcohol use, physical activity, oral contraceptives use, menopause, and each riboflavin intake from the 4 most used food sources including cereals, vegetables, meats, and eggs, and supplementary sources.

**Table 3.** ORs (95% CI) of variables according to riboflavin intake after adjusting for covariates in pre- and post-menopausal women

| | | Pre-menopausal women | | | Post-menopausal women | | |
|---|---|---|---|---|---|---|---|
| | | Riboflavin intake (mg/day) | | | Riboflavin intake (mg/day) | | |
| | | ≥1.2 | <1.2 | | ≥1.2 | <1.2 | |
| Variables | Model | OR | OR (95% CI) | *p* value | OR | OR (95% CI) | *p* value |
| Hypertension | 1[†] | 1 | 1.00 (0.66-1.50) | 0.986 | 1 | 1.57 (1.28-1.94) | <0.001 |
| | 2[‡] | 1 | 1.07 (0.68-1.70) | 0.768 | 1 | 1.48 (1.16-1.89) | 0.002 |
| Diabetic mellitus | 1 | 1 | 1.94 (1.20-3.16) | 0.007 | 1 | 1.43 (1.08-1.89) | 0.013 |
| | 2 | 1 | 1.66 (1.07-2.59) | 0.024 | 1 | 1.43 (1.05-1.93) | 0.022 |
| Dyslipidemia | 1 | 1 | 1.16 (0.86-1.58) | 0.335 | 1 | 1.13 (0.92-1.39) | 0.234 |
| | 2 | 1 | 1.23 (0.88-1.73) | 0.231 | 1 | 1.09 (0.87-1.37) | 0.455 |
| Central obesity | 1 | 1 | 0.95 (0.73-1.22) | 0.670 | 1 | 1.37 (1.09-1.70) | 0.006 |
| | 2 | 1 | 1.01 (0.77-1.31) | 0.956 | 1 | 1.32 (1.02-1.70) | 0.035 |
| Blood pressure (mmHg): systolic ≥130 or diastolic ≥85 or medication for hypertension | 1 | 1 | 0.93 (0.68-1.28) | 0.659 | 1 | 1.44 (1.17-1.77) | < 0.001 |
| | 2 | 1 | 1.01 (0.72-1.41) | 0.974 | 1 | 1.40 (1.10-1.77) | 0.006 |
| Fasting blood glucose (mg/dL): ≥100 or medication for diabetes | 1 | 1 | 1.36 (1.03-1.79) | 0.030 | 1 | 1.24 (0.98-1.56) | 0.070 |
| | 2 | 1 | 1.38 (1.03-1.85) | 0.029 | 1 | 1.18 (0.92-1.51) | 0.206 |
| Triglycerides (mg/dL) ≥150 | 1 | 1 | 1.11 (0.82-1.51) | 0.484 | 1 | 1.11 (0.87-1.42) | 0.414 |
| | 2 | 1 | 1.23 (0.89-1.72) | 0.215 | 1 | 0.94 (0.73-1.23) | 0.662 |
| HDL-cholesterol (mg/dL) <50 | 1 | 1 | 1.15 (0.92-1.44) | 0.212 | 1 | 1.06 (0.85-1.32) | 0.603 |
| | 2 | 1 | 1.15 (0.91-1.45) | 0.251 | 1 | 0.97 (0.76-1.22) | 0.773 |
| Metabolic syndrome | 1 | 1 | 1.10 (0.79-1.53) | 0.588 | 1 | 1.40 (1.11-1.76) | 0.004 |
| | 2 | 1 | 1.15 (0.80-1.67) | 0.449 | 1 | 1.30 (1.01-1.69) | 0.045 |

HDL: high-density lipoprotein
[†]Model 1: adjusted for age.
[‡]Model 2: adjusted for age, alcohol use, physical activity, oral contraceptives use, menopause, and each riboflavin intake from the 4 most used food sources including cereals, vegetables, meats, and eggs, and supplementary sources.

mation caused by oxidative stress.[16]

There was a significant and positive relationship between insufficient riboflavin intake and hypertension in women, particularly in post-menopausal women. Like our study, riboflavin intake was inversely associated with BP in participants aged 40-59 years.[25] In another study, McNulty et al. have suggested that riboflavin helped modulate BP by lowering concentrations of homocysteine, particularly in individuals with a specific genotype.[26] Riboflavin modulates concentrations of plasma homocysteine,[27] a risk factor for CVD.[28]

Meanwhile, Mazidi et al have suggested that higher intake of specific nutrients, including riboflavin, all together was associated with lower prevalence of MetS and central obesity, with adverse effects on TGs and HDL-cholesterol concentrations,[29] but a single linked nutrient could not be identified. Our study showed that sufficient intake of riboflavin, as a single nutrient, might help lower the prevalence of MetS and other cardiometabolic risks, and our findings underscore the potential therapeutic and protective effects of riboflavin intake against the development of MetS, especially in women. We also found that poor riboflavin intake contributed partially to low HDL-cholesterol for men. Furthermore, the findings of associations between riboflavin intake and central obesity are remarkable, given the evidence that WC in post-menopausal women had higher risk for CVD-related mortality than other components of MetS.[30]

We believe that our findings of the sex-based effects on cardiometabolic risks are important in regard to public health concerns. The findings of our study have been supported by Chang et al. who showed that increased medical costs in men with MetS were more evident than women among Taiwanese elders.[31] Possible mechanisms surrounding the sex-specific effects of riboflavin on MetS include differences in regional distribution of body fat, including visceral and subcutaneous fat and composition of sex hormones, including oestrogen.32 Cartier et al. have suggested a similar mechanism that inflammatory markers are influenced by intra-abdominal adiposity in men and mainly by subcutaneous adiposity in women.[32] Moreover, changes in body fat composition, including increased accumulation of abdominal adipose tissue and age-related decreased sex hormone concentrations, may help explain the age- or menopause-related effects of riboflavin on the prevalence of MetS in this study.

We considered the RNI for riboflavin in adults as 1.5 mg for men and 1.2 mg for women. These concentrations are 120% of the EAR, determined by applying a 10% coefficient of variation, based on the KDRI.[12] Here, the EAR is the daily nutrient intake concentrations necessary to meet the requirements of half of the apparently healthy individuals in a target group. The EAR of riboflavin was established after considering that its intake helps maintain normal erythrocyte glutathione reductase activity and urinary excretion of riboflavin without causing clinical deficiencies.

The use of dietary supplements for achieving recommended intakes has recently been widespread, with approximately half of the Korea adults consuming dietary supplements. In 2016, 41.4% of men and 51.0% of women reportedly consumed dietary supplements containing micronutrients regularly in the past 1 year.[7] Therefore, the present study estimated total riboflavin intake from both foods and supplementary sources. The study by Choi et al showed that urinary riboflavin excretion was positively correlated with total riboflavin intake, rather than only food intake.[33] Urinary riboflavin concentrations reflect tissue saturation under optimal riboflavin status, given that the excess riboflavin supplied into human body is not stored and it is likely to be removed quickly by renal secretion.6 Therefore, total riboflavin intake might be a means of estimating urinary excretion of riboflavin, potentially reflecting riboflavin status.[34,35] As indicated previously, riboflavin is present in various food sources. Milk and dairy products are the main sources of its intake in Western countries.[36] Recent nationwide nutrition surveys in Korea have reported that meat and meat products, followed by cereals and grains, make the greatest contribution to riboflavin intake in men, whereas the principal sources are eggs and vegetables in women.[7] These differences in dietary habits could reportedly be one possible reason for the sex-based discrepancies in the associations of insufficient riboflavin intake with cardiometabolic risks in the present study. Cardiometabolic risks are reportedly associated with excessive energy intake. Most of the energy consumed by the Korean population is derived from grains and meat.[7] Indeed, the habitual consumptions of meat and grains, as main sources of riboflavin, were reported higher for men than women. Another possibility is that a higher frequency of eating out, probably with energy-rich foods, was more evident in Korea men than in women; 44.3% for men and 23.2% for women in 2016.[7] Therefore, it seems that the association of insufficient riboflavin intake and cardiometabolic risks is influenced in certain circumstances depending on food habitual cultures or personal behaviours; further studies evaluating these possibilities are required.

This study has several limitations. We cannot conclude a temporal relationship between daily riboflavin intake and cardiometabolic risks as our study included a cross-sectional design. Thus, we cannot determine if riboflavin intake concentrations preceded the development of MetS or its individual components. Since some data in our study were based on self-reports, there could be a response bias. Specifically, negative behaviours could be under-reported and their importance to cardiometabolic risks therefore under-estimated. The 24-h dietary recall method may not fully reflect long-term habitual dietary behaviours. However, this concern is mitigated by the large sample size, thus increasing statistical power and the probability of revealing diverse dietary behaviours. The possibility of other confounders from unmeasured variables such as intake of other residual nutrients cannot be completely ruled out and requires strictly separate in-depth analyses in further research.

Despite these limitations, to the best of our knowledge, this is the first study to evaluate the sex-based differences in the association between insufficient riboflavin intake and cardiometabolic risks, including MetS, using current data obtained from a large representative Korean population. Few studies have evaluated the effect of riboflavin on cardiometabolic conditions according to menopausal status. Thus, more interventional studies are needed to

determine the mechanisms of sex-based differences related to riboflavin activities in humans.

In conclusion, we found a significant sex-specific association between insufficient intake of riboflavin and cardiometabolic risk in Korean adults. These findings underscore the importance of implementing sex-specific dietary education or counselling interventions, including sufficient riboflavin intake. The findings of this study may provide evidence to support improving public policies and assistance programmes that target at-risk groups, potentially reducing the burden of MetS and its cardiometabolic consequences.

## AUTHOR DISCLOSURES

The authors declare that there are no conflicts of interest.

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## Supplmentary Tables

**Supplementary Table 1.** General characteristics of men and women, according to metabolic syndrome

| Variables[†] | Men | | | | Women | | | |
|---|---|---|---|---|---|---|---|---|
| | Metabolic syndrome | | Total | *p* value[‡] | Metabolic syndrome | | Total | *p* value |
| | Yes | No | | | Yes | No | | |
| Total | 654 (28.5) | 1369 (71.5) | 2023 (100.0) | | 1123 (23.5) | 2916 (76.5) | 4039 (100.0) | |
| Age (years) | | | | <0.001 | | | | <0.001 |
| 19-29 | 18 (5.3) | 208 (24.5) | 226 (19.1) | | 10 (1.7) | 383 (20.0) | 393 (15.7) | |
| 30-39 | 44 (11.9) | 162 (16.8) | 206 (15.4) | | 51 (6.0) | 560 (19.4) | 611 (16.2) | |
| 40-49 | 83 (19.8) | 206 (18.4) | 289 (18.8) | | 116 (12.7) | 644 (23.0) | 760 (20.6) | |
| 50-59 | 116 (23.9) | 221 (17.8) | 337 (19.5) | | 237 (25.1) | 583 (19.7) | 820 (21.0) | |
| 60-69 | 189 (19.2) | 282 (11.2) | 471 (13.5) | | 326 (25.1) | 428 (10.5) | 754 (13.9) | |
| ≥70 | 204 (19.8) | 290 (11.3) | 494 (13.7) | | 383 (29.4) | 318 (7.5) | 701 (12.7) | |
| Alcohol use | | | | <0.001 | | | | 0.004 |
| Yes | 99 (17.2) | 138 (10.0) | 237 (12.1) | | 21 (1.9) | 109 (4.0) | 130 (3.5) | |
| No | 555 (82.8) | 1231 (90.0) | 1786 (87.9) | | 1102 (98.1) | 2807 (96.0) | 3909 (96.5) | |
| Regular physical activity | | | | 0.003 | | | | <0.001 |
| Yes | 298 (51.4) | 744 (60.1) | 1042 (57.6) | | 365 (35.4) | 1396 (51.4) | 1761 (47.7) | |
| No | 356 (48.6) | 625 (39.9) | 981 (42.4) | | 758 (64.6) | 1520 (48.6) | 2278 (52.3) | |
| Oral contraceptive use | | | | | | | | <0.001 |
| Yes | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 281 (23.5) | 483 (15.5) | 764 (17.4) | |
| No | 654 (100.0) | 1369 (100.0) | 2023 (100.0) | | 842 (76.5) | 2433 (84.5) | 3275 (82.6) | |
| Menopause | | | | | | | | <0.001 |
| Yes | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 919 (76.8) | 1275 (36.0) | 2194 (45.5) | |
| No | 654 (100.0) | 1369 (100.0) | 2023 (100.0) | | 204 (23.2) | 1641 (64.0) | 1845 (54.5) | |
| Hypertension | | | | <0.001 | | | | <0.001 |
| Yes | 450 (61.6) | 356 (19.4) | 806 (31.4) | | 744 (62.1) | 492 (13.2) | 1236 (24.7) | |
| No | 204 (38.4) | 1013 (80.6) | 1217 (68.6) | | 379 (37.9) | 2424 (86.8) | 2803 (75.3) | |
| Diabetic mellitus | | | | <0.001 | | | | <0.001 |
| Yes | 204 (25.3) | 108 (5.0) | 312 (10.8) | | 337 (28.8) | 110 (3.1) | 447 (9.1) | |
| No | 450 (74.7) | 1261 (95.0) | 1711 (89.2) | | 786 (71.2) | 2806 (96.9) | 3592 (90.9) | |
| Dyslipidemia | | | | <0.001 | | | | <0.001 |
| Yes | 368 (60.4) | 325 (21.6) | 693 (32.7) | | 640 (58.9) | 659 (19.4) | 1299 (28.7) | |
| No | 286 (39.6) | 1044 (78.4) | 1330 (67.3) | | 483 (41.1) | 2257 (80.6) | 2740 (71.3) | |
| Central obesity | | | | <0.001 | | | | <0.001 |
| Yes | 453 (71.7) | 206 (15.4) | 659 (31.4) | | 797 (70.9) | 424 (13.0) | 1221 (26.6) | |
| No | 201 (28.3) | 1163 (84.6) | 1364 (68.6) | | 326 (29.1) | 2492 (87.0) | 2818 (73.4) | |
| Blood pressure (mmHg): systolic ≥130 or diastolic ≥85 or medication for hypertension | | | | <0.001 | | | | <0.001 |
| Yes | 546 (80.5) | 497 (29.7) | 1043 (44.2) | | 886 (75.9) | 651 (18.0) | 1537 (31.6) | |
| No | 108 (19.5) | 872 (70.3) | 980 (55.8) | | 237 (24.1) | 2265 (82.0) | 2502 (68.4) | |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
[†]Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
[‡]*p* values are from Rao-scott $\chi^2$ test or ANOVA.

**Supplementary Table 1.** General characteristics of men and women, according to metabolic syndrome (cont.)

| Variables† | Men | | | | Women | | | |
|---|---|---|---|---|---|---|---|---|
| | Metabolic syndrome | | Total | *p* value‡ | Metabolic syndrome | | Total | *p* value |
| | Yes | No | | | Yes | No | | |
| Fasting blood glucose (mg/dL): ≥100 or medication for diabetes | | | | <0.001 | | | | <0.001 |
| Yes | 512 (73.5) | 390 (22.6) | 902 (37.1) | | 790 (70.0) | 442 (13.8) | 1232 (27.0) | |
| No | 142 (26.5) | 979 (77.4) | 1121 (62.9) | | 333 (30.0) | 2474 (86.2) | 2807 (73.0) | |
| Triglycerides (mg/dL) ≥150 | | | | <0.001 | | | | <0.001 |
| Yes | 450 (73.3) | 236 (18.2) | 686 (33.9) | | 646 (59.4) | 262 (7.9) | 908 (20.0) | |
| No | 204 (26.7) | 1133 (81.8) | 1337 (66.1) | | 477 (40.6) | 2654 (92.1) | 3131 (80.0) | |
| HDL-cholesterol (mg/dL): men <40, women <50 | | | | <0.001 | | | | <0.001 |
| Yes | 348 (52.9) | 168 (11.5) | 516 (23.3) | | 890 (79.1) | 767 (24.5) | 1657 (37.3) | |
| No | 306 (47.1) | 1201 (88.5) | 1507 (76.7) | | 233 (20.9) | 2149 (75.5) | 2382 (62.7) | |
| BMI (kg/m²) | 27.1±0.18 | 23.6±0.09 | 24.6±0.10 | <0.001 | 26.4±0.12 | 22.4±0.07 | 23.4±0.07 | <0.001 |
| Waist circumference (cm) | 93.8±0.41 | 83.4±0.23 | 86.4±0.25 | <0.001 | 88.4±0.32 | 76.2±0.21 | 79.1±0.23 | <0.001 |
| Systolic blood pressure (mmHg) | 128±0.60 | 117±0.42 | 120±0.38 | <0.001 | 128±0.60 | 112±0.31 | 115±0.33 | <0.001 |
| Diastolic blood pressure (mmHg) | 81.5±0.47 | 76.2±0.29 | 77.7±0.26 | <0.001 | 77.1±0.36 | 71.9±0.20 | 73.1±0.19 | <0.001 |
| Fasting blood glucose (mg/dL) | 115±1.58 | 95.7±0.48 | 101±0.69 | <0.001 | 113±1.04 | 92.3±0.31 | 97.1±0.41 | <0.001 |
| Total cholesterol (mg/dL) | 194±1.96 | 188±1.17 | 190±1.05 | 0.008 | 197±1.44 | 192±0.78 | 193±0.69 | 0.002 |
| Triglycerides (mg/dL) | 232±9.75 | 114±2.20 | 148±3.55 | <0.001 | 183±3.80 | 90.6±1.01 | 112±1.46 | <0.001 |
| LDL- cholesterol (mg/dL) | 109±1.81 | 115±1.01 | 113±0.94 | 0.004 | 116±1.29 | 116±0.72 | 116±0.62 | 0.897 |
| HDL- cholesterol (mg/dL) | 41.3±0.42 | 50.6±0.33 | 47.9±0.28 | <0.001 | 44.7±0.31 | 58.1±0.28 | 55.0±0.26 | <0.001 |
| Total energy intake (kcal/day) | 2348±50.6 | 2419±34.1 | 2399±29.2 | 0.225 | 1596±23.8 | 1754±15.7 | 1717±13.6 | <0.001 |
| Carbohydrates intake (g/day) | 354±7.45 | 349±4.23 | 350±3.73 | 0.579 | 273±4.41 | 273±2.53 | 273±2.30 | 0.986 |
| Protein intake (g/day) | 80.7±1.90 | 89.4±2.31 | 87.0±1.74 | 0.003 | 52.8±0.93 | 62.3±0.77 | 60.1±0.64 | <0.001 |
| Fat intake (g/day) | 49.6±2.02 | 58.6±1.71 | 56.0±1.39 | <0.001 | 29.6±0.82 | 41.6±0.66 | 38.8±0.57 | <0.001 |
| SFA intake (g/day) | 14.2±0.70 | 16.9±0.52 | 16.1±0.42 | 0.002 | 8.24±0.26 | 11.9±0.20 | 11.0±0.17 | <0.001 |
| MUFA intake (g/day) | 15.8±0.79 | 19.0±0.61 | 18.1±0.50 | 0.001 | 9.21±0.31 | 13.2±0.23 | 12.2±0.20 | <0.001 |
| PUFA intake (g/day) | 12.4±0.46 | 14.6±0.50 | 13.9±0.40 | <0.001 | 7.60±0.22 | 10.4±0.20 | 9.74±0.17 | <0.001 |
| Dietary fiber intake (g/day) | 27.6±0.69 | 26.5±0.46 | 26.8±0.40 | 0.147 | 22.1±0.44 | 21.9±0.31 | 22.0±0.26 | 0.752 |
| Total riboflavin intake (mg/day) | 1.53±0.05 | 1.65±0.04 | 1.61±0.03 | 0.038 | 1.05±0.02 | 1.25±0.02 | 1.21±0.01 | <0.001 |
| Sources of riboflavin intake (mg/day) | | | | | | | | |
| Cereals and grains | 0.25±0.02 | 0.27±0.01 | 0.27±0.01 | 0.977 | 0.17±0.01 | 0.19±0.00 | 0.18±0.00 | <0.001 |
| Meats | 0.19±0.01 | 0.25±0.01 | 0.23±0.01 | <0.001 | 0.10±0.01 | 0.16±0.01 | 0.15±0.00 | <0.001 |
| Vegetables | 0.26±0.01 | 0.24±0.01 | 0.24±0.01 | 0.089 | 0.21±0.01 | 0.18±0.00 | 0.19±0.00 | 0.002 |
| Eggs | 0.21±0.02 | 0.21±0.01 | 0.21±0.01 | 0.221 | 0.15±0.01 | 0.21±0.01 | 0.20±0.01 | <0.001 |
| Fruits | 0.06±0.00 | 0.06±0.00 | 0.06±0.00 | 0.773 | 0.06±0.00 | 0.06±0.00 | 0.06±0.00 | 0.154 |
| Dairy products | 0.10±0.01 | 0.12±0.01 | 0.11±0.01 | 0.209 | 0.08±0.01 | 0.11±0.00 | 0.10±0.00 | <0.001 |
| Supplements | 0.46±0.05 | 0.49±0.04 | 0.48±0.02 | 0.529 | 0.27±0.00 | 0.33±0.00 | 0.32±0.00 | <0.001 |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
†Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
‡*p* values are from Rao-scott $\chi^2$ test or ANOVA.

**Supplementary Table 2.** General characteristics of pre- and post-menopausal women, according to metabolic syndrome

| Variables[†] | Pre-menopausal women | | | | Post-menopausal women | | | |
|---|---|---|---|---|---|---|---|---|
| | Metabolic syndrome | | Total | *p* value[‡] | Metabolic syndrome | | Total | *p* value |
| | Yes | No | | | Yes | No | | |
| Total | 204 (10.0) | 1641 (90.0) | 1845 (100) | | 919 (39.6) | 1275 (60.4) | 2194 (100) | |
| Age (years) | | | | <0.001 | | | | <0.001 |
| 19-29 | 10 (7.1) | 383 (31.2) | 393 (28.8) | | 0 (0.0) | 0 (0.0) | 0 (0.0) | |
| 30-39 | 51 (26.0) | 558 (30.2) | 609 (29.7) | | 0 (0.0) | 2 (0.1) | 2 (0.1) | |
| 40-49 | 104 (48.0) | 597 (33.1) | 701 (34.6) | | 12 (2.0) | 47 (5.0) | 59 (3.8) | |
| 50-59 | 38 (18.8) | 101 (5.5) | 139 (6.8) | | 199 (27.0) | 482 (45.0) | 681 (37.9) | |
| 60-69 | 1 (0.0) | 0 (0.0) | 1 (0.0) | | 325 (32.7) | 428 (29.2) | 753 (30.6) | |
| ≥70 | 0 (0.0) | 2 (0.1) | 2 (0.1) | | 383 (38.3) | 316 (20.8) | 699 (27.7) | |
| Alcohol use | | | | 0.171 | | | | 0.621 |
| Yes | 7 (3.0) | 90 (5.5) | 97 (5.3) | | 14 (1.6) | 19 (1.3) | 33 (1.4) | |
| No | 197 (97.0) | 1551 (94.5) | 1748 (94.7) | | 905 (98.4) | 1256 (98.7) | 2161 (98.6) | |
| Regular physical activity | | | | 0.073 | | | | <0.001 |
| Yes | 92 (45.7) | 833 (53.2) | 925 (52.5) | | 273 (32.3) | 563 (48.3) | 836 (41.9) | |
| No | 112 (54.3) | 808 (46.8) | 920 (47.5) | | 646 (67.7) | 712 (51.7) | 1358 (58.1) | |
| Oral contraceptive use | | | | 0.389 | | | | 0.002 |
| Yes | 33 (15.6) | 215 (13.2) | 248 (13.4) | | 248 (25.8) | 268 (19.6) | 516 (22.0) | |
| No | 171 (84.4) | 1426 (86.8) | 1597 (86.6) | | 671 (74.2) | 1007 (80.4) | 1678 (78.0) | |
| Hypertension | | | | <0.001 | | | | <0.001 |
| Yes | 66 (30.1) | 76 (4.1) | 142 (6.7) | | 678 (71.7) | 416 (29.3) | 1094 (46.1) | |
| No | 138 (69.9) | 1565 (95.9) | 1703 (93.3) | | 241 (28.3) | 859 (70.7) | 1100 (53.9) | |
| Diabetic mellitus | | | | <0.001 | | | | <0.001 |
| Yes | 40 (17.7) | 13 (0.7) | 53 (2.4) | | 297 (32.1) | 97 (7.2) | 394 (17.1) | |
| No | 164 (82.3) | 1628 (99.3) | 1792 (97.6) | | 622 (67.9) | 1178 (92.8) | 1800 (82.9) | |
| Dyslipidemia | | | | <0.001 | | | | <0.001 |
| Yes | 98 (52.9) | 144 (7.6) | 242 (12.1) | | 542 (60.6) | 515 (40.5) | 1057 (48.5) | |
| No | 106 (47.1) | 1497 (92.4) | 1603 (87.9) | | 377 (39.4) | 760 (59.5) | 1137 (51.5) | |
| Central obesity | | | | <0.001 | | | | <0.001 |
| Yes | 156 (75.8) | 173 (10.1) | 329 (16.7) | | 641 (69.4) | 251 (18.2) | 892 (38.5) | |
| No | 48 (24.2) | 1468 (89.9) | 1516 (83.3) | | 278 (30.6) | 1024 (81.8) | 1302 (61.5) | |
| Blood pressure (mmHg): systolic ≥130 or diastolic ≥85 or medication for hypertension | | | | <0.001 | | | | <0.001 |
| Yes | 106 (50.2) | 144 (8.0) | 250 (12.2) | | 780 (83.7) | 507 (35.9) | 1287 (54.8) | |
| No | 98 (49.8) | 1497 (92.0) | 1595 (87.8) | | 139 (16.3) | 768 (64.1) | 907 (45.2) | |
| Fasting blood glucose (mg/dL): ≥100 or medication for diabetes | | | | <0.001 | | | | <0.001 |
| Yes | 143 (68.9) | 147 (8.5) | 290 (14.5) | | 647 (70.3) | 295 (23.2) | 942 (41.9) | |
| No | 61 (31.1) | 1494 (91.5) | 1555 (85.5) | | 272 (29.7) | 980 (76.8) | 1252 (58.1) | |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
[†]Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
[‡]*p* values are from Rao-scott $\chi^2$ test or ANOVA.

**Supplementary Table 2.** General characteristics of pre- and post-menopausal women, according to metabolic syndrome (cont.)

| Variables† | Pre-menopausal women | | | | Post-menopausal women | | | |
|---|---|---|---|---|---|---|---|---|
| | Metabolic syndrome | | Total | *p* value‡ | Metabolic syndrome | | Total | *p* value |
| | Yes | No | | | Yes | No | | |
| Triglycerides (mg/dL) ≥150 | | | | <0.001 | | | | <0.001 |
| Yes | 128 (69.0) | 115 (6.4) | 243 (12.7) | | 518 (56.5) | 147 (10.5) | 665 (28.7) | |
| No | 76 (31.0) | 1526 (93.6) | 1602 (87.3) | | 401 (43.5) | 1128 (89.5) | 1529 (71.3) | |
| HDL-cholesterol (mg/dL) <50 | | | | <0.001 | | | | <0.001 |
| Yes | 175 (83.9) | 414 (23.7) | 589 (29.7) | | 715 (77.6) | 353 (25.9) | 1068 (46.4) | |
| No | 29 (16.1) | 1227 (76.3) | 1256 (70.3) | | 204 (22.4) | 922 (74.1) | 1126 (53.6) | |
| BMI (kg/m²) | 27.5±0.32 | 22.1±0.08 | 22.6±0.10 | <0.001 | 26.0±0.12 | 23.1±0.10 | 24.3±0.09 | <0.001 |
| Waist circumference (cm) | 89.5±0.70 | 74.6±0.25 | 76.1±0.28 | <0.001 | 88.1±0.35 | 79.1±0.27 | 82.6±0.28 | <0.001 |
| Systolic blood pressure (mmHg) | 120±1.21 | 107±0.31 | 108±0.32 | <0.001 | 130±0.64 | 120±0.58 | 124±0.44 | <0.001 |
| Diastolic blood pressure (mmHg) | 80.0±0.83 | 70.8±0.25 | 71.7±0.26 | <0.001 | 76.2±0.36 | 73.9±0.32 | 74.9±0.24 | <0.001 |
| Fasting Blood glucose (mg/dL) | 111±1.98 | 90.1±0.33 | 92.1±0.40 | <0.001 | 114±1.24 | 96.3±0.55 | 103±0.64 | <0.001 |
| Total cholesterol (mg/dL) | 203±3.16 | 185±0.91 | 187±0.91 | <0.001 | 195±1.53 | 203±1.28 | 200±0.98 | <0.001 |
| Triglycerides (mg/dL) | 205±9.31 | 84.2±1.20 | 96.3±1.68 | <0.001 | 177±3.70 | 102±1.56 | 132±2.02 | <0.001 |
| LDL-cholesterol (mg/dL) | 118±2.66 | 110±0.79 | 111±0.78 | 0.003 | 115±1.41 | 125±1.21 | 121±0.91 | <0.001 |
| HDL-cholesterol (mg/dL) | 43.9±0.69 | 58.5±0.37 | 57.0±0.36 | <0.001 | 44.9±0.35 | 57.5±0.42 | 52.5±0.34 | <0.001 |
| Total energy intake (kcal/day) | 1792±56.2 | 1809±19.6 | 1807±18.44 | 0.781 | 1536±22.6 | 1657±22.3 | 1610±16.0 | <0.001 |
| Carbohydrates intake (g/day) | 282±9.79 | 268±3.03 | 270±2.93 | 0.177 | 270.4±4.35 | 282.1±3.61 | 278±2.83 | 0.036 |
| Protein intake (g/day) | 61.7±2.17 | 65.6±0.96 | 65.2±0.88 | 0.108 | 50.1±0.99 | 56.5±1.05 | 54.0±0.75 | <0.001 |
| Fat intake (g/day) | 42.3±1.97 | 47.1±0.85 | 46.6±0.81 | 0.023 | 25.7±0.76 | 31.9±0.96 | 29.5±0.66 | <0.001 |
| SFA intake (g/day) | 12.3±0.70 | 13.8±0.28 | 13.6±0.26 | 0.044 | 7.02±0.21 | 8.47±0.25 | 7.89±0.17 | <0.001 |
| MUFA intake (g/day) | 14.0±0.79 | 15.2±0.30 | 15.1±0.28 | 0.142 | 7.78±0.28 | 9.60±0.32 | 8.88±0.23 | <0.001 |
| PUFA intake (g/day) | 10.1±0.50 | 11.3±0.26 | 11.2±0.24 | 0.035 | 6.84±0.23 | 8.86±0.32 | 8.06±0.21 | <0.001 |
| Dietary fiber intake (g/day) | 21.7±0.99 | 20.4±0.35 | 20.5±0.33 | 0.225 | 22.2±0.49 | 24.6±0.46 | 23.7±0.34 | <0.001 |
| Total riboflavin intake (mg/day) | 1.19±0.04 | 1.31±0.02 | 1.30±0.02 | 0.007 | 1.00±0.03 | 1.16±0.03 | 1.10±0.02 | <0.001 |
| Sources of riboflavin intake (mg/day) | | | | | | | | |
| Cereals and grains | 0.20±0.04 | 0.21±0.01 | 0.21±0.01 | 0.084 | 0.17±0.02 | 0.17±0.00 | 0.16±0.00 | 0.574 |
| Meats | 0.16±0.02 | 0.19±0.01 | 0.19±0.01 | 0.097 | 0.08±0.01 | 0.10±0.01 | 0.09±0.00 | 0.082 |
| Vegetables | 0.19±0.01 | 0.17±0.00 | 0.17±0.00 | 0.016 | 0.22±0.01 | 0.20±0.01 | 0.21±0.01 | 0.372 |
| Eggs | 0.22±0.03 | 0.23±0.01 | 0.23±0.01 | 0.674 | 0.13±0.01 | 0.18±0.01 | 0.16±0.01 | <0.001 |
| Fruits | 0.06±0.01 | 0.06±0.00 | 0.06±0.00 | 0.845 | 0.06±0.00 | 0.08±0.00 | 0.07±0.00 | <0.001 |
| Dairy products | 0.08±0.01 | 0.12±0.01 | 0.11±0.01 | 0.018 | 0.07±0.01 | 0.09±0.01 | 0.08±0.00 | 0.049 |
| Supplements | 0.29±0.03 | 0.34±0.00 | 0.34±0.00 | 0.059 | 0.27±0.01 | 0.33±0.03 | 0.30±0.00 | 0.054 |

HDL: high-density lipoprotein; BMI: Body Mass Index; LDL: low-density lipoprotein; SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.
†Categorical variable: unweighted n (weighted %), continuous variable: mean±standard error.
‡*p* values are from Rao-scott $\chi^2$ test or ANOVA.