



## Eating rate and prevalence of metabolic syndrome in Japanese

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-005241
Article Type:	Research
Date Submitted by the Author:	11-Mar-2014
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<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, PREVENTIVE MEDICINE, PUBLIC HEALTH

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Manuscripts

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6 **1 Eating rate and prevalence of metabolic syndrome in Japanese**  
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15 Keywords: eating rate, eating speed, metabolic syndrome, health check, Japan

16 Word count: 2354

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17 **ABSTRACT**

18 **Objectives:** To examine the association between eating rate and the prevalence of  
19 metabolic syndrome.

20 **Design:** Cross-sectional study.

21 **Setting:** Annual health checkup for workers at a health check service center in Japan.

22 **Participants:** A total of 56,865 participants (41,820 males and 15,045 females) who  
23 attended health checkup in 2011 and reported not to have a history of coronary heart  
24 disease or stroke.

25 **Main outcome measure:** Metabolic syndrome was defined according to two criteria:  
26 the Adult Treatment Program III of the National Cholesterol Education Program  
27 (NCEP-ATPIII) and International Diabetes Federation (IDF).

28 **Results:** In multiple logistic regression models, eating rate was significantly and  
29 positively associated with metabolic syndrome defined by both criteria. The odds ratio  
30 (95% confidence interval) for slow, normal and fast were 0.70 (0.62 to 0.79), 1.00  
31 (reference) and 1.61 (1.53 to 1.70), respectively in men (P for trend <0.001), and 0.74  
32 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
33 trend <0.001) under NCEP-ATPIII criteria. The association of eating rate and metabolic  
34 syndrome was attenuated after further adjustment for body mass index, but remained

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6 35 statistically significant only in men. Of components of metabolic syndrome, the  
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9 36 strongest association with eating rate was abdominal obesity. The associations of slow  
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12 37 eating with high blood pressure and hyperglycemia and those of fast eating with  
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15 38 abnormal lipid profile were still significant in men, even after adjustment for body mass  
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18 39 index.

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21 40 **Conclusions:** Our results suggest that eating rate is associated with higher prevalence of  
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24 41 metabolic syndrome and that this association is largely accounted for by higher body  
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6 43 **Strength and Limitation**  
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9 44 This large scale study was the first study to elucidate the association between eating rate  
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12 45 and metabolic syndrome in men and women, separately.  
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15 46 This is the only study to report the association between eating rate and metabolic  
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18 47 syndrome defined by using waist circumference.  
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21 48 Eating rate was assessed by self-report questionnaire.  
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## 49 Introduction

50 Metabolic syndrome (MetS) is a cluster of physiological risk factors associated  
51 with cardiovascular disease and several types of cancer.<sup>1</sup> Determination of etiologic  
52 factors for MetS is required for the establishment of public health strategies to reduce its  
53 prevalence and prevent resulting complications. Growing evidence from both  
54 observational and interventional studies in human suggests a role of dietary habits in the  
55 development of MetS,<sup>2-4</sup> which originates from obesity. Obesity has been extensively  
56 investigated in relation to dietary habits including eating rate since 1962, when Ferster  
57 published a theoretical and practical weight control program focusing on eating  
58 behaviors including eating rate.<sup>5</sup> Observational studies showed that obese people ate at a  
59 faster rate than non-obese people,<sup>6</sup> and reducing eating rate may be a simple and  
60 effective therapy for obesity.<sup>7</sup>

61 During the past decade, several cross-sectional studies have found a positive  
62 association between eating rate and overweight<sup>8-11</sup> or insulin resistance.<sup>11-15</sup> Similarly, a  
63 few longitudinal studies showed that eating fast was associated with an increased risk of  
64 weight gain<sup>16, 17</sup> and type 2 diabetes.<sup>18</sup> In addition, some cross-sectional studies have  
65 reported that fast eating was positively associated with hypertriglyceridemia and low  
66 high-density lipoprotein cholesterol (HDL-C).<sup>11, 14, 19</sup> Therefore it is conceivable that

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6 67 eating rate may be associated with the prevalence of MetS. To our knowledge, however,  
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9 68 only one Korean study cross-sectionally examined eating rate in relation to MetS.<sup>20</sup> In  
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12 69 that study, MetS was defined by using body mass index (BMI), rather than waist  
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15 70 circumference, and investigated the association in men only. Waist circumference is a  
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18 71 component of most MetS definitions<sup>21, 22</sup> as a surrogate of central obesity, which can  
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21 72 better predict cardiovascular risk.<sup>23</sup> It is therefore necessary to examine the relationship  
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24 73 between eating rate and MetS using waist circumference in both sexes. Here, we  
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27 74 investigated cross-sectionally the association between eating rate and the prevalence of  
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30 75 MetS according to two criteria: the National Cholesterol Education Program, Adult  
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33 76 Treatment Panel III (NCEP-ATPIII) criteria<sup>21</sup> and International Diabetes Federation  
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36 77 (IDF) criteria<sup>22</sup> using a large dataset of worker health checkup in Japanese men and  
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39 78 women.  
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## 43 44 80 **METHODS AND PROCEDURES**

### 45 46 47 81 **Study population**

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49 82 Study participants were attendants of 2011 (calendar year) annual health  
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52 83 examination at All Japan Labor Welfare Foundation (Tokyo), a health service center  
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55 84 performing health checkup for employees. Participants were employees and their  
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6 85 dependents, aged 17-99 in men and 17-85 in women. Of 297,148 participants, we  
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9 86 excluded 3,660 with a history of myocardial infarction, coronary heart disease or stroke,  
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12 87 24,452 with missing information on eating rate, 192,581 who took meal within 8 hours  
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15 88 or provided no information on meal time, 204,423 with missing data for any of the  
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18 89 components of MetS, 15,886 with missing information on covariates (BMI, smoking  
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21 90 status, alcohol consumption and physical activity). Some participants met more than one  
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24 91 of these exclusion criteria, leaving 56,865 participants (41,820 males and 15,045  
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27 92 females) for analysis.

#### 93 94 **Data collection and measurements**

95 In Japan, a new health checkup program focusing on MetS was initiated in  
96 2008 according to the recommendation from the Ministry of Health, Labor and  
97 Welfare.<sup>24</sup> At All Japan Labor Welfare Foundation, a self-administered questionnaire,  
98 which was recommended by the Japanese government (Ministry of Health, Labor and  
99 Welfare),<sup>25</sup> was used to assess eating rate, medical history and health-related lifestyles  
100 including smoking, alcohol consumption and regular physical activity. Eating rate was  
101 assessed by asking “How fast is your speed of eating?”, with three response options  
102 (slow, normal and fast). A trained staff measured height to the nearest 0.1 cm, weight to



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6 103 the nearest 0.1 kg and waist circumference to the nearest 0.1 cm at the umbilical level in  
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9 104 a standing position. BMI was calculated as the weight in kilograms divided by the  
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12 105 squared height in meters. Blood pressure in the sitting position was measured using an  
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15 106 automated machine (HEM-907, Omron, Kyoto, Japan). Participants with high blood  
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18 107 pressure ( $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic) received another measurement  
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21 108 and data showing lower systolic blood pressure was used. Venous blood sample was  
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24 109 collected, stored in a cooler at 4 degrees for transportation to an external laboratory  
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27 110 (SRL, Tokyo, Japan) and measured within 24 hours of blood drawing. Triglyceride level  
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30 111 was measured by enzymatic colorimetric test (Bio Majesty JCA-BM8060, JEOL, Tokyo,  
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33 112 Japan). HDL-C level was determined by a direct method (Bio Majesty JCA-BM8060,  
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36 113 JEOL, Tokyo, Japan). Plasma glucose levels were determined using by the hexokinase  
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39 114 method (an automatic clinical chemistry analyzer JCA-BM9000 series, JEOL, Tokyo,  
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42 115 Japan).

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#### 45 46 117 **Definitions for MetS**

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49 118 MetS was defined according to two criteria: NCEP-ATPIII criteria and IDF  
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52 119 criteria. Under NCEP-ATPIII criteria, MetS was defined as the presence of three or  
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55 120 more of the following risk factors: 1) waist circumference for Asian population  $\geq 90$  cm  
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6 121 in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3)  
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9 122 HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women,  
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12 123 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  
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15 124  $\geq 100$  mg/dL (5.6 mmol/L).<sup>21</sup> To meet the criteria for IDF MetS, participants must have  
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18 125 central obesity (waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women) plus any  
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21 126 two of the following factors: 1) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$   
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23 127 mg/dL (1.29 mmol/L) in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3)  
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26 128 blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 4) fasting glucose level  
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29 129  $\geq 100$  mg/dL (5.6 mmol/L).<sup>22</sup> In both criteria, participants under medication for diabetes,  
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32 130 hypertension and dyslipidemia were considered as having respective factor, irrespective  
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35 131 of measured data.  
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41 133 **Statistical analysis**

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44 134 Participants were divided into three groups according to eating rate (slow,  
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47 135 normal and fast). The characteristics of participants across eating rate categories were  
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50 136 expressed as means (standard deviation), medians (interquartile range) and percentages  
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53 137 for normal continuous variables, non-normal continuous variables and categorical  
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56 138 variables, respectively. Trend association was assessed by assigning ordinal numbers (0  
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6 139 to 2) to the categories of eating rate (slow, normal and fast, respectively) and was tested  
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9 140 using linear regression and an extension of the Wilcoxon Rank-Sum test for normal and  
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12 141 non-normal continuous variables, respectively, and logistic regression for categorical  
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15 142 variables. Multiple logistic regression analysis was used to estimate the odds ratios  
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18 143 (OR) and 95% confidence interval (CI) for the prevalence of MetS across eating rate  
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21 144 categories, with normal eating rate as the reference. In multiple regression analysis, the  
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24 145 initial model was adjusted for age (continuous, year) only. In the second model, we  
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27 146 further adjusted for smoking status (non-smoker, daily smoker consuming <20  
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29 147 cigarettes per day or  $\geq 20$  cigarettes per day), alcohol consumption (non-drinker, <1 *go*,  
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32 148 1 to <2 *go* or  $\geq 2$  *go* per day; *go* is a Japanese traditional unit of measurement for alcohol  
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35 149 and a *go* of sake (Japanese traditional beverage) contains ~23g of ethanol) and physical  
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38 150 activity (walking time <60 min per day or  $\geq 60$  min per day). In the third model, we  
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41 151 added BMI (continuous,  $\text{kg/m}^2$ ) to the second model. We performed likelihood ratio test  
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44 152 for testing the interaction between eating rate and sex. All analyses were done for men  
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47 153 and women separately because the interaction was significant (P for interaction <0.001).  
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50 154 We repeated the above analyses for each component of MetS. Two-tailed P value <0.05  
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53 155 was considered statistically significant. All statistical analyses were performed with  
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56 156 STATA, version 12.1 (StataCorp, College Station, TX, USA).

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89 158 **RESULTS**

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12 159 The prevalence of MetS defined by NCEP-ATPIII and IDF was 18.5% and  
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14 160 12.8%, respectively, in men and 12.9% and 11.4%, respectively, in women. **Table 1**  
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17 161 shows characteristics of the study participants across categories of eating rate. Men who  
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20 162 ate fast tended to be young, whereas women who ate slowly tended to be young. Those  
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23 163 who ate fast had significantly higher BMI, waist circumference, triglyceride level and  
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26 164 systolic and diastolic blood pressures and lower HDL-C level in both men and women.  
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29 165 The ORs of the prevalence of MetS across eating rate are shown in **Table 2**.  
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32 166 Regardless of which criteria we used, faster eating was associated with higher  
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35 167 prevalence of MetS in age- and multivariable-adjusted models. The trend was more  
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38 168 apparent in men than in women under IDF criteria. The multivariable-adjusted ORs  
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41 169 (95% CI) of MetS for eating slow, normal and fast rate were 0.70 (0.62 to 0.79), 1.00  
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44 170 (reference) and 1.61 (1.53 to 1.70), respectively, in men (P for trend <0.001), and 0.74  
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47 171 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
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50 172 trend <0.001) under NCEP-ATPIII criteria; the correspondent values were 0.62 (0.54 to  
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53 173 0.72), 1.00 (reference) and 1.82 (1.72 to 1.94), respectively, in men (P for trend <0.001),  
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56 174 and 0.73 (0.58 to 0.91), 1.00 (reference) and 1.32 (1.17 to 1.49), respectively, in women  
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6 175 (P for trend <0.001) under IDF criteria. Further adjustment for BMI markedly  
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9 176 attenuated these associations; however, the association with eating rate and MetS under  
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12 177 both criteria remained statistically significant in men.  
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15 **Table 3** shows the ORs of the prevalence of individual MetS components  
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18 179 across three categories of eating rate. The prevalence of central obesity increased from  
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21 180 slow to fast eating in both men and women (OR 0.63, 1.00 (reference) and 1.97,  
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24 181 respectively, in men (P for trend <0.001), and 0.73, 1.00(reference) and 1.44,  
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27 182 respectively, in women (P for trend <0.001)). High blood pressure was positively  
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30 183 associated with eating rate in both sexes. Eating rate was associated with fasting glucose,  
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33 184 triglyceride and HDL-C in men and with HDL-C in women. Additional adjustment for  
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36 185 BMI largely attenuated these associations, but the associations of slow eating with high  
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39 186 blood pressure (men and women) and hyperglycemia (men) and those of fast eating  
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42 187 with abnormal lipid profile (men) remained statistically significant.  
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## 45 46 47 189 **DISCUSSION**

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50 190 In this large population of Japanese men and women, we found that eating rate  
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53 191 was positively associated with the prevalence of MetS, especially in men. Of  
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56 192 components of MetS, the association with abdominal obesity was strongest. The  
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6 193 relationship with blood pressure in both sexes and fasting plasma glucose and lipids in  
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9 194 men remained statistically significant even after additional adjustment for BMI. To our  
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12 195 best knowledge, the present study is the first to report a positive association between  
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15 196 eating rate and the prevalence of MetS defined by using waist circumference.

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18 197 The present finding for Mets is consistent with that of a study among Korean  
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21 198 men reporting that eating rate was positively associated with MetS, which was defined  
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24 199 by using BMI instead of waist circumference.<sup>20</sup> As regards MetS components, our study  
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27 200 is compatible with some cross-sectional studies showing that eating rate was associated  
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30 201 with higher BMI<sup>8-10</sup> and two longitudinal studies showing that eating rate was  
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33 202 associated with weight gain.<sup>16, 17</sup> In a Korean study that elucidated the association  
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36 203 between eating rate and components of MetS for men and women separately, eating rate  
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39 204 was associated with obesity, high blood pressure, hyperglycemia and abnormal lipid  
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42 205 profile in men, whereas it was associated with only obesity in women.<sup>11</sup> Our results  
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45 206 were largely consistent with those in the Korean study (except for blood pressure in  
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48 207 women).

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50 208 We found that the association between eating rate and MetS was stronger in  
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53 209 men than in women. In the present study, the association between eating rate and MetS  
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56 210 components (hyperglycemia with slow eating and dyslipidemia with fast eating)

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6 211 remained statistically significant even after adjusting for BMI in men but not in women.  
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9 212 This finding appears to be compatible with those in previous studies showing sex  
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12 213 difference in association of eating rate with MetS components<sup>11</sup> and insulin resistance.<sup>12</sup>  
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15 214 These results may reflect the difference in actual eating speed between men and women.  
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18 215 One study elucidated that women took more bites, smaller bite size and slower bites  
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21 216 than men in eating the same amount of doughnut, irrespectively of body size.<sup>26</sup> Another  
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24 217 study showed that objectively measured eating speed in men with self-reported slow  
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27 218 eating was faster than that in women with self-reported fast eating.<sup>27</sup> Taken together,  
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30 219 eating rate may have a greater impact on metabolism in men than that in women.

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32 220 Although mechanisms whereby eating rate influences metabolism is not fully  
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35 221 elucidated, overeating may link fast eating to MetS. Fast eating gives few satiety signal  
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38 222 from oral cavity to the brain,<sup>28, 29</sup> induces less satiation and satiety due to a lack of  
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41 223 stomach expansion<sup>30</sup> and alters the circulating levels of certain gut hormones.<sup>31, 32</sup> In  
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44 224 these pathways, fast eating leads to excess energy intake,<sup>33, 34</sup> resulting in overweight  
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47 225 and MetS. Because fast eating has been associated with obesity even after adjusting for  
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50 226 total energy intake,<sup>8-11, 14</sup> there may be other pathways. One study showed that  
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53 227 interleukin-1 $\beta$  and interleukin-6 were higher among those who ate fast than among  
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56 228 those who ate slowly, even after accounting for energy intake and BMI.<sup>35</sup> The authors

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6 229 ascribed the elevation of these inflammatory cytokines to an increased postprandial  
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9 230 hyperglycemia after eating fast. These cytokines were well-known to give rise to obesity,  
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11 231 dyslipidemia and insulin resistance,<sup>36-39</sup> and thus also accounted for the association  
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14 232 between fast eating and MetS.  
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18 233 The strengths of our study deserve mention. Data of this large-scale study was  
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20 234 derived from annual health-checkup for employees of various companies. Therefore, the  
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22 235 present findings may be applicable to apparently healthy workers in Japan. In addition,  
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24 236 body weight, body height and waist circumference was measured by trained technicians,  
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26 237 which increased the validity of our study. Nonetheless, several limitations in the present  
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28 238 study merit consideration. First, eating rate was self-reported. However, self-reported  
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30 239 eating rate has been shown to be well correlated with friend-reported one<sup>9</sup> or objectively  
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32 240 measured one.<sup>27</sup> Second, total energy intake was not available in our study. However,  
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34 241 because energy intake is influenced by eating rate and thus may act as a mediator rather  
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36 242 than confounder, the adjustment of energy intake could underestimate the association  
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38 243 between eating rate and MetS. Moreover, eating rate has been associated with body  
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40 244 weight independent of energy intake.<sup>7-10, 13</sup> Third, cross-sectional design precludes any  
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42 245 causal inferences about the role of eating rate. Finally, we cannot exclude a possibility  
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44 246 of the effects of residual confounding and confounding by unmeasured variables.  
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6 247 In conclusion, we found a positive trend association between eating rate and  
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9 248 the prevalence of MetS, especially in men. The association between eating rate and  
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12 249 MetS was largely accounted for by level of obesity, only eating rate per se may have  
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15 250 small effect, in any, on the components of MetS. Further research should address  
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18 251 whether reducing eating rate prevents obesity and MetS.  
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Table 1. Characteristics of the study individuals according to eating rates

	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Age (years) <sup>b</sup>	46.9 ± 12.3	46.9 ± 10.9	45.0 ± 10.4	<0.001	43.5 ± 12.5	47.2 ± 11.6	46.7 ± 11.2	<0.001
Walking time, ≥60 min/day (%)	21.8	19.0	20.6	0.004	15.5	15.0	16.1	0.798
Smoking status (%)								
Non-smoker	61.9	55.0	56.6	<0.001	82.9	83.1	80.7	0.572
Daily consuming <20 cigarettes /day	28.6	34.6	31.3		16.0	15.7	17.6	
Daily consuming ≥20 cigarettes /day	9.5	10.4	12.1		1.1	1.2	1.7	

## Alcohol (%)

Non-drinker	30.2	26.7	26.7	<0.001	53.4	52.2	49.8	<0.001
Drinker <1 <i>go</i> /day <sup>d</sup>	33.9	35.7	34.5		34.2	35.9	35.5	
Drinker 1 to <2 <i>go</i> /day <sup>d</sup>	24.6	26.3	26.8		9.5	9.5	11.5	
Drinker $\geq 2$ <i>go</i> /day <sup>d</sup>	11.3	11.3	12.0		2.9	2.4	3.2	
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	22.4 $\pm$ 3.3	23.4 $\pm$ 3.3	24.6 $\pm$ 3.7	<0.001	21.0 $\pm$ 3.5	21.8 $\pm$ 3.5	22.5 $\pm$ 3.8	<0.001
Waist circumference (cm) <sup>b</sup>	80.3 $\pm$ 9.2	82.9 $\pm$ 9.0	86.0 $\pm$ 9.8	<0.001	75.5 $\pm$ 9.5	77.7 $\pm$ 9.4	79.6 $\pm$ 9.8	<0.001
Systolic blood pressure (mm Hg) <sup>b</sup>	123.5 $\pm$ 15.5	126.1 $\pm$ 15.5	126.7 $\pm$ 15.1	<0.001	113.1 $\pm$ 16.3	117.3 $\pm$ 17.2	117.0 $\pm$ 17.2	<0.001
Diastolic blood pressure (mm Hg) <sup>b</sup>	75.2 $\pm$ 11.4	77.3 $\pm$ 11.9	78.0 $\pm$ 12.0	<0.001	69.1 $\pm$ 10.9	71.4 $\pm$ 11.5	71.5 $\pm$ 11.9	<0.001
Fasting plasma glucose (mg/dL) <sup>c</sup>	91 (85 to 98)	92 (86 to 99)	92 (86 to 99)	0.001	87 (82 to 93)	88 (83 to 94)	88 (83 to 94)	0.001
Triglyceride (mg/dL) <sup>c</sup>	92 (65 to 138)	99 (69 to 148)	107 (73 to 161)	<0.001	63 (48 to 87)	69 (51 to 96)	71 (52 to 101)	<0.001

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HDL-C (mg/dL) <sup>b</sup>	61.3 ± 15.3	59.4 ± 15.0	57.2 ± 14.3	<0.001	71.4 ± 15.3	70.5 ± 15.8	69.3 ± 15.5	<0.001
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Cross to sectional survey of 56,865 examinees in All Japan Labor Welfare Foundation, Japan, 2011.

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Linear regression and an extension of the Wilcoxon Rank-Sum test for normal and non-normal continuous variables, respectively, and logistic regression for categorical variables, assigning ordinal number (0 to 2) to eating rate.

<sup>b</sup> Mean ± SD.

<sup>c</sup> Median (interquartile range).

<sup>d</sup> One go contains ~23g of ethanol.

Table 2. Odds ratios and 95% confidence intervals for metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (25.0)	
NCEP-ATPIII								
MetS, n	361	4,180	3,193		116	1,261	547	
Model 1 <sup>b</sup>	0.70(0.62 to 0.79)	1.00 (Ref)	1.62(1.53 to 1.71)	<0.001	0.75(0.61 to 0.92)	1.00 (Ref)	1.27(1.13 to 1.42)	<0.001
Model 2 <sup>c</sup>	0.70(0.62 to 0.79)	1.00 (Ref)	1.61(1.53 to 1.70)	<0.001	0.74(0.60 to 0.91)	1.00 (Ref)	1.27(1.13 to 1.43)	<0.001
Model 3 <sup>d</sup>	0.91(0.80 to 1.04)	1.00 (Ref)	1.10(1.03 to 1.17)	<0.001	0.88(0.70 to 1.11)	1.00 (Ref)	0.98(0.86 to 1.12)	0.714
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MetS, n	205	2,727	2,450		101	1,115	504	
Model 1 <sup>b</sup>	0.62(0.54 to 0.72)	1.00 (Ref)	1.84(1.73 to 1.95)	<0.001	0.73(0.59 to 0.92)	1.00 (Ref)	1.32(1.17 to 1.49)	<0.001
Model 2 <sup>c</sup>	0.62(0.54 to 0.72)	1.00 (Ref)	1.82(1.72 to 1.94)	<0.001	0.73(0.58 to 0.91)	1.00 (Ref)	1.32(1.17 to 1.49)	<0.001
Model 3 <sup>d</sup>	0.81(0.67 to 0.97)	1.00 (Ref)	1.15(1.07 to 1.24)	<0.001	0.87(0.68 to 1.12)	1.00 (Ref)	1.00(0.87 to 1.14)	0.553

NCEP-ATPIII= the National Cholesterol Education Program, Adult Treatment Panel III: the presence of three or more of the following risk factors:

- 1) waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L); Ref=Reference; IDF= International Diabetes Federation: waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women, and any two of the following factors: 1) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.29 mmol/L) in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7mmol/L), 3) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 4) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L).

<sup>a</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>b</sup> Adjusted for age.

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Table 3. Odds ratios and 95% confidence intervals for components of metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	slow	normal	fast		slow	normal	fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Central obesity <sup>b</sup>								
Model 1 <sup>c</sup>	0.63(0.56 to 0.71)	1.00 (Ref)	1.98(1.89 to 2.08)	<0.001	0.73(0.64 to 0.83)	1.00 (Ref)	1.44(1.34 to 1.56)	<0.001
Model 2 <sup>d</sup>	0.63(0.56 to 0.70)	1.00 (Ref)	1.97(1.88 to 2.07)	<0.001	0.73(0.64 to 0.83)	1.00 (Ref)	1.44(1.33 to 1.56)	<0.001
High blood pressure <sup>e</sup>								
Model 1 <sup>c</sup>	0.75(0.69 to 0.82)	1.00 (Ref)	1.22(1.17 to 1.27)	<0.001	0.76(0.66 to 0.88)	1.00 (Ref)	1.10(1.01 to 1.21)	<0.001
Model 2 <sup>d</sup>	0.74(0.68 to 0.81)	1.00 (Ref)	1.20(1.15 to 1.26)	<0.001	0.76(0.65 to 0.88)	1.00 (Ref)	1.10(1.00 to 1.20)	<0.001



Model 3 <sup>f</sup>	0.88(0.81 to 0.96)	1.00 (Ref)	0.97(0.93 to 1.02)	0.645	0.85(0.72 to 0.99)	1.00 (Ref)	0.93(0.84 to 1.02)	0.923
High fasting plasma glucose <sup>g</sup>								
Model 1 <sup>c</sup>	0.78(0.71 to 0.87)	1.00 (Ref)	1.17(1.12 to 1.23)	<0.001	1.03(0.85 to 1.25)	1.00 (Ref)	1.17(1.04 to 1.31)	0.035
Model 2 <sup>d</sup>	0.78(0.71 to 0.87)	1.00 (Ref)	1.16(1.11 to 1.22)	<0.001	1.03(0.85 to 1.25)	1.00 (Ref)	1.16(1.03 to 1.31)	0.042
Model 3 <sup>f</sup>	0.88(0.80 to 0.98)	1.00 (Ref)	0.99(0.94 to 1.05)	0.238	1.14(0.94 to 1.40)	1.00 (Ref)	1.02(0.90 to 1.15)	0.536
High triglyceride <sup>h</sup>								
Model 1 <sup>c</sup>	0.88(0.80 to 0.96)	1.00 (Ref)	1.32(1.26 to 1.38)	<0.001	0.83(0.67 to 1.01)	1.00 (Ref)	1.14(1.01 to 1.28)	0.002
Model 2 <sup>d</sup>	0.90(0.82 to 0.98)	1.00 (Ref)	1.33(1.27 to 1.39)	<0.001	0.81(0.66 to 1.00)	1.00 (Ref)	1.13(1.01 to 1.27)	0.002
Model 3 <sup>f</sup>	1.08(0.98 to 1.19)	1.00 (Ref)	1.07(1.02 to 1.12)	0.121	0.90(0.73 to 1.11)	1.00 (Ref)	0.98(0.87 to 1.11)	0.753
Low HDL-C <sup>i</sup>								
Model 1 <sup>c</sup>	0.83(0.73 to 0.96)	1.00 (Ref)	1.34(1.26 to 1.43)	<0.001	0.90 (0.74 to 1.09)	1.00 (Ref)	1.11(0.99 to 1.25)	0.018

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Model 2 <sup>d</sup>	0.83(0.73 to 0.96)	1.00 (Ref)	1.36(1.28 to 1.45)	<0.001	0.89(0.74 to 1.08)	1.00 (Ref)	1.12(1.00 to 1.26)	0.011
Model 3 <sup>f</sup>	0.97(0.84 to 1.12)	1.00 (Ref)	1.10(1.03 to 1.18)	0.004	1.00(0.82 to 1.22)	1.00 (Ref)	0.96(0.85 to 1.08)	0.500

Ref=Reference; BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>b</sup> Waist circumference  $\geq 90$  cm in men,  $\geq 80$  cm in women.

<sup>c</sup> Adjusted for age.

<sup>d</sup> Adjusted for age, smoking status, alcohol, and regular physical activity.

<sup>e</sup> Blood pressure  $\geq 130$  mm Hg for systolic or  $\geq 85$  mm Hg for diastolic.

<sup>f</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.

<sup>g</sup> Fasting plasma glucose  $\geq 100$  mg/dL or under medication.

<sup>h</sup> Triglyceride  $\geq 150$  mg/dL or under medication.

<sup>i</sup> HDL-C  $< 40$  mg/dL in men,  $< 50$  mg/dL in women or under medication.

## Acknowledgments

The authors would like to thank Dr. Nobuo Yanagisawa and Dr. Takeshi Kawaguchi for their coordinating the study.

Contributors: SN and KKurotani designed study and drafted the manuscript. SN, NMP, AN, KKuwahara performed the data analysis. MD collected and interpreted the data. All authors have participated in the interpretation of the findings, revised it critically for important intellectual content and approved final version to be published. TM and YN provided administrative, technical and material support. SN and TM are guarantors.

Funding: This study was supported by the Industrial Health Foundation.

Competing interests: All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: all authors declare no interests.

Ethical approval: The research protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine and the Ethics Committee of Toho University.

Data sharing: No additional data available.

Transparency: SN affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant,

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

MS ID#: BMJ.2014.018520

MS TITLE: Eating rate and prevalence of metabolic syndrome in Japanese.

	Item No	Recommendation	Location in manuscript
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	Line 20 on page 2
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	What was done: line 18-19 on page 2 What was found: line 40-42 on page 2
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Scientific background: line 50-73 on page 5 Rationale: Line 73-78 on page 5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	Line 67-68 and line 77-78 on page 6
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	Line 74 on page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Line 82-85 on page 6-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Line 85-92 on page 7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Line 118-150 on page 8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Line 100-102 on page 7
Bias	9	Describe any efforts to address potential sources of bias	Exclusion: line 85-92 on page 7 Adjustment: line 145-151 on page 10
Study size	10	Explain how the study size was arrived at	Not provided
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Line 144-151 on page 10

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4	Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
5			Line 134-156 on page 9-10
6			(b) Describe any methods used to examine subgroups and interactions
7			Line 151-153 on page 10
8			(c) Explain how missing data were addressed
9			We excluded participants who had missing information on potential confounding variables (line 89 on page 7).
10			(d) If applicable, describe analytical methods taking account of sampling strategy
11			N/A
12			(e) Describe any sensitivity analyses
13			N/A
14	<b>Results</b>		
15	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
16			Line 159-160 on page 11
17			Table 1
18			(b) Give reasons for non-participation at each stage
19			N/A
20			(c) Consider use of a flow diagram
21			N/A
22	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
23			Table 1
24			Line 159-164 on page 11
25			(b) Indicate number of participants with missing data for each variable of interest
26			N/A
27	Outcome data	15*	Report numbers of outcome events or summary measures
28			Table 2
29			Line 159-160 on page 11
30	Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
31			Table 2, Table3
32			Line 165-187 on page 11-12
33			(b) Report category boundaries when continuous variables were categorized
34			Table2, Table3
35			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
36			N/A
37	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
38			Line 152-153 on page 10
39	<b>Discussion</b>		
40	Key results	18	Summarise key results with reference to study objectives
41			Line 190-194 on page 12-13
42	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias
43			Line 237-246 on page 15

		or imprecision. Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Line 197-219 on page 13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	Line 247-251 on page 16
<b>Other information</b>			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	This study was supported by the Industrial Health Foundation for drafting the manuscript.

N/A: Not applicable.

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-005241.R1
Article Type:	Research
Date Submitted by the Author:	31-May-2014
Complete List of Authors:	Nagahama, Satsue; All Japan Labor Welfare Foundation, ; School of Medicine, Toho University, Department of Environmental and Occupational Health Kurotani, Kayo; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Pham, Ngoc Minh; Thai Nguyen University of Medicine and Pharmacy, Department of Epidemiology, Faculty of Public Health Nanri, Akiko; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Kuwahara, Keisuke; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Dan, Masashi; All Japan Labor Welfare Foundation, Department of Epidemiology and Prevention, Center for Clinical Sciences Nishiwaki, Yuji; School of Medicine, Toho University, Department of Environmental and Occupational Health Mizoue, Tetsuya; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences
<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, PREVENTIVE MEDICINE, PUBLIC HEALTH

SCHOLARONE™  
Manuscripts

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6 1 **Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional**  
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14 4 Satsue Nagahama <sup>1 2 3\*</sup>, Kayo Kurotani <sup>1</sup>, Ngoc Minh Pham <sup>4</sup>, Akiko Nanri <sup>1</sup>, Keisuke  
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52 17 Keywords: eating rate, metabolic syndrome, health checkup, Japan, Joint Interim  
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55 18 Statement  
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19 Word count: 2373

For peer review only

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6 20 **ABSTRACT**  
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9 21 **Objectives:** To examine the association between self-reported eating rate and metabolic  
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12 22 syndrome.

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15 23 **Design:** Cross-sectional study.  
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18 24 **Setting:** Annual health checkup at a health check service center in Japan.  
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21 25 **Participants:** A total of 56,865 participants (41,820 males and 15,045 females) who  
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24 26 attended health checkup in 2011 and reported not to have a history of coronary heart  
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26 27 disease or stroke.  
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29 28 **Main outcome measure:** Metabolic syndrome was defined by the joint of interim  
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32 29 statement of the International Diabetes Federation and the American Heart  
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35 30 Association/National Heart, Lung, and Blood Institute.  
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38 31 **Results:** In multiple logistic regression models, eating rate was significantly and  
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41 32 positively associated with metabolic syndrome. The multivariable-adjusted odds ratios  
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44 33 (95% confidence interval) for slow, normal and fast were 0.70 (0.62 to 0.79), 1.00  
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47 34 (reference) and 1.61 (1.53 to 1.70), respectively, in men (P for trend <0.001), and 0.74  
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50 35 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
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53 36 trend <0.001). The association of eating rate and metabolic syndrome was attenuated  
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56 37 after further adjustment for body mass index in both sexes, but remained statistically  
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6 38 significant in men. Of metabolic syndrome components, abdominal obesity showed the  
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9 39 strongest association with eating rate. The associations of slow eating with high blood  
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12 40 pressure and hyperglycemia and that of fast eating with lipid abnormality were still  
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15 41 significant in men, even after adjustment for body mass index.  
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18 42 **Conclusions:** Results suggest that eating rate is associated with the presence of  
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21 43 metabolic syndrome and that this association is largely accounted for by the difference  
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24 44 of body mass according to eating rate.  
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6 45 **Strength and Limitation**  
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9 46 This study included a large number of participants, used waist circumference in defining  
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12 47 metabolic syndrome, and analyzed data for men and women separately.

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15 48 Eating rate was assessed by a self-reported questionnaire. Information on dietary intake  
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18 49 was not obtained.  
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Metabolic syndrome (MetS) is a cluster of physiological risk factors associated with cardiovascular disease and several types of cancer.<sup>1</sup> Determination of etiologic factors for MetS is required for the establishment of public health strategies to reduce its prevalence and prevent resulting complications. Growing evidence from both observational and interventional studies suggests a role of dietary habits in the development of MetS,<sup>2-4</sup> which originates from obesity. Obesity has been extensively investigated in relation to dietary habits including eating rate since 1962, when Ferster published a theoretical and practical weight control program focusing on eating behaviors including eating rate.<sup>5</sup> Observational studies showed that obese people ate at a faster rate than non-obese people,<sup>6</sup> and reducing eating rate may be a simple and effective therapy for obesity.<sup>7</sup>

During the past decade, several cross-sectional studies have found a positive association between eating rate and overweight<sup>8-11</sup> or insulin resistance.<sup>11-15</sup> Similarly, a few longitudinal studies showed that eating fast was associated with an increased risk of weight gain<sup>16, 17</sup> and type 2 diabetes.<sup>18</sup> In addition, some cross-sectional studies have reported that fast eating was positively associated with hypertriglyceridemia and low high-density lipoprotein cholesterol (HDL-C).<sup>11, 14, 19</sup> Therefore it is conceivable that

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6 68 eating rate may be associated with MetS. To our knowledge, however, only one Korean  
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9 69 study cross-sectionally examined eating rate in relation to MetS.<sup>20</sup> In that study, MetS  
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12 70 was defined by using body mass index (BMI), rather than waist circumference, and  
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15 71 investigated the association in men only. Waist circumference is a component of most  
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18 72 MetS definitions as a surrogate of central obesity, which can better predict  
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21 73 cardiovascular risk.<sup>21</sup> It is therefore necessary to examine the relationship between  
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24 74 eating rate and MetS using waist circumference in both sexes. Here, we investigated  
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27 75 cross-sectionally the association between self-reported eating rate and the presence of  
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30 76 MetS according to the joint of interim statement of the International Diabetes Federation  
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33 77 and the American Heart Association/National Heart, Lung, and Blood Institute (JIS)<sup>22</sup>  
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36 78 using a large dataset of health checkup in Japanese men and women.  
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## 80 **METHODS AND PROCEDURES**

### 81 **Study population**

82 In Japan, health checkup under occupational health and safety law is mandatory  
83 for all employed workers<sup>23</sup> and has been modified in 2008 when the recommendation  
84 for new national health checkup system focusing on MetS has been launched.<sup>24</sup> Study  
85 participants were attendants of 2011 (calendar year) annual health checkup at All Japan

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6 86 Labor Welfare Foundation (Tokyo), a health service center performing health checkup.  
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9 87 Participants were mainly Japanese employees but also included a small number of their  
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12 88 dependents and foreign workers, aged 17-99 in men and 17-85 in women. Of 297,148  
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15 89 participants, we excluded 3,660 with a history of myocardial infarction, coronary heart  
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18 90 disease or stroke, 24,452 with missing information on eating rate, 192,581 who took  
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21 91 meal within 8 hours or provided no information on meal time, 204,423 with missing  
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24 92 data for any of the components of MetS, 15,886 with missing information on covariates  
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27 93 (BMI, smoking status, alcohol consumption and physical activity). Some participants  
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30 94 met more than one of these exclusion criteria, leaving 56,865 participants (41,820 males  
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33 95 and 15,045 females) for analysis. We did not obtain written informed consent from each  
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36 96 participant; instead, we disclosed the execution of the study by showing posters, giving  
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39 97 participants an opportunity to refuse the use of their data for the study. This procedure  
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42 98 conforms to the Japanese Ethical Guidelines for Epidemiological Research. The  
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45 99 research protocol was approved by the Ethics Committee of the National Center for  
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48 100 Global Health and Medicine and the Ethics Committee of Toho University.

#### 101 **Data collection and measurements**

102 A self-administered questionnaire, which was recommended for specific health  
103 examination by the Japanese government (Ministry of Health, Labour and Welfare),<sup>25</sup>

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6 104 was used to assess eating rate, medical history and health-related lifestyles including  
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9 105 smoking, alcohol consumption and regular physical activity. Eating rate was assessed by  
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12 106 asking “How fast is your speed of eating?”, with three response options (slow, normal  
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15 107 and fast). A trained staff measured height to the nearest 0.1 cm, weight to the nearest 0.1  
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18 108 kg and waist circumference to the nearest 0.1 cm at the umbilical level in a standing  
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21 109 position. BMI was calculated as the weight in kilograms divided by the squared height  
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24 110 in meters. Blood pressure in the sitting position was measured using an automated  
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27 111 machine (HEM-907, Omron, Kyoto, Japan). Participants with high blood pressure  
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30 112 ( $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic) received another measurement and data  
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33 113 showing lower systolic blood pressure was used. Venous blood sample was collected,  
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36 114 stored in a cooler at 4 degrees for transportation to an external laboratory (SRL, Tokyo,  
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39 115 Japan) and measured within 24 hours of blood drawing. Triglyceride level was  
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42 116 measured by enzymatic colorimetric test (Bio Majesty JCA-BM8060, JEOL, Tokyo,  
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45 117 Japan). HDL-C level was determined by a direct method (Bio Majesty JCA-BM8060,  
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48 118 JEOL, Tokyo, Japan). Plasma glucose levels were determined using by the hexokinase  
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51 119 method (an automatic clinical chemistry analyzer JCA-BM9000 series, JEOL, Tokyo,  
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54 120 Japan).

55 121 **Definitions for MetS**  
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6 122 According to the JIS criteria, MetS was defined as three or more of the  
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9 123 following risk factors: 1) waist circumference for Asian population  $\geq 90$  cm in men and  
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12 124  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$   
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15 125 mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood  
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18 126 pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$   
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21 127 mg/dL (5.6 mmol/L).<sup>22</sup> Participants under medication for diabetes, hypertension and  
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24 128 dyslipidemia were considered as having respective factor, irrespective of measured data.

### 25 26 129 **Statistical analysis**

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29 130 Participants were divided into three groups according to eating rate (slow,  
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32 131 normal and fast). The characteristics of participants across eating rate categories were  
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35 132 expressed as means (standard deviation) for continuous variables and percentages for  
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38 133 categorical variables, respectively. Fasting plasma glucose and triglyceride were  
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41 134 expressed as medians (interquartile range) due to their skewed distribution. Trend  
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44 135 association was assessed by assigning ordinal numbers (0 to 2) to the categories of  
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47 136 eating rate (slow, normal and fast, respectively) and was tested using linear regression,  
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50 137 an extension of the Wilcoxon Rank-Sum test and logistic regression, as appropriate.  
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53 138 Multiple logistic regression analysis was used to estimate the odds ratios (OR) with  
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56 139 95% confidence intervals (CI) for the presence of MetS across eating rate categories,  
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6 140 with normal eating rate as the reference. We adjusted for age (continuous, year) in the  
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9 141 basic model. In the second model, we further adjusted for smoking status (non-smoker,  
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12 142 daily smoker consuming <20 cigarettes per day or  $\geq 20$  cigarettes per day), physical  
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15 143 activity (walking time <60 min per day or  $\geq 60$  min per day), and alcohol consumption  
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18 144 (non-drinker, <1 *go*, 1 to <2 *go* or  $\geq 2$  *go* per day; one *go* of sake, Japanese traditional  
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21 145 beverage, is about 180 ml of 10 to 14% of ethanol and contains ~23g of ethanol). In the  
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24 146 third model, we added BMI (continuous,  $\text{kg/m}^2$ ) to the second model. We performed  
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27 147 likelihood ratio test for testing the interaction between eating rate and sex. All analyses  
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30 148 were done for men and women separately because the interaction was significant (P for  
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33 149 interaction <0.001). We repeated the above analyses for each component of MetS.  
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36 150 Two-tailed P value <0.05 was considered statistically significant. All statistical analyses  
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39 151 were performed with STATA, version 12.1 (StataCorp, College Station, TX, USA).

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## 42 43 44 153 **RESULTS**

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47 154 The prevalence of MetS was 18.5% in men and 12.9% in women. **Table 1**  
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50 155 shows characteristics of the study participants across categories of eating rate. Men who  
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53 156 ate fast tended to be young, whereas women who ate slowly tended to be young. Those  
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56 157 who ate fast had significantly higher BMI, waist circumference, triglyceride level and

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6 158 systolic and diastolic blood pressures and lower HDL-C level in both men and women.  
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9 159 The ORs of the presence of MetS across eating rate are shown in **Table 2**.

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11 160 Faster eating was associated with higher presence of MetS in age- and

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15 161 multivariable-adjusted models. The trend was more apparent in men than in women.

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17 162 The multivariable-adjusted ORs (95% CI) of MetS for eating slow, normal and fast rate

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20 163 were 0.70 (0.62 to 0.79), 1.00 (reference) and 1.61 (1.53 to 1.70), respectively, in men

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23 164 (P for trend <0.001), and 0.74 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43),

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26 165 respectively, in women (P for trend <0.001). Further adjustment for BMI markedly

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29 166 attenuated these associations; however, the association with fast eating and MetS

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32 167 remained statistically significant in men.  
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35 168 **Table 3** shows the ORs of the presence of individual MetS components across

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38 169 three categories of eating rate. The ORs of central obesity increased from slow to fast

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41 170 eating in both men and women (OR 0.63, 1.00 (reference) and 1.97, respectively, in men

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44 171 (P for trend <0.001), and 0.73, 1.00(reference) and 1.44, respectively, in women (P for

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47 172 trend <0.001)). High blood pressure and triglyceride were positively associated with

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50 173 eating rate in both sexes. High fasting plasma glucose and low HDL-C were associated

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53 174 with slow eating in both sexes, but they were associated with fast eating in men only.

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55 175 Additional adjustment for BMI largely attenuated these associations, but the  
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6 176 associations of slow eating with high blood pressure (men and women) and  
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9 177 hyperglycemia (men) and those of fast eating with abnormal lipid profile (men)  
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12 178 remained statistically significant.

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## 16 17 18 180 **DISCUSSION**

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20 181 In this large population of Japanese men and women, we found that eating rate  
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23 182 was positively associated with the presence of MetS, especially in men. Of components  
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26 183 of MetS, the association with abdominal obesity was strongest. The relationship with  
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29 184 blood pressure in both sexes and fasting plasma glucose and lipids in men remained  
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32 185 statistically significant even after additional adjustment for BMI. To our best knowledge,  
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35 186 the present study is the first to report a positive association between eating rate and  
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38 187 MetS defined by using waist circumference.

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41 188 The present finding for MetS is consistent with that of a study among Korean  
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44 189 men reporting that eating rate was positively associated with MetS, which was defined  
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47 190 by using BMI instead of waist circumference.<sup>20</sup> As regards MetS components, our study  
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50 191 is compatible with some cross-sectional studies showing that eating rate was associated  
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53 192 with higher BMI<sup>8-10</sup> and two longitudinal studies showing that eating rate was  
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56 193 associated with weight gain.<sup>16, 17</sup> In a Korean study that elucidated the association  
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6 194 between eating rate and components of MetS for men and women separately, eating rate  
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9 195 was associated with obesity, high blood pressure, hyperglycemia and abnormal lipid  
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12 196 profile in men, whereas it was associated with only obesity in women.<sup>11</sup> Our results  
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15 197 were largely consistent with those in the Korean study (except for blood pressure in  
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18 198 women).

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21 199 Notably, we found that the associations of MetS components with eating rate  
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24 200 were largely attenuated after adjustment for BMI, a finding compatible with those of a  
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27 201 cross-sectional study in Korea<sup>11</sup> and a prospective study in Japan.<sup>18</sup> This result indicates  
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30 202 that obesity is a mediator whereby fast eating deteriorates MetS components. We also  
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33 203 found, however, that some associations remained statistically significant even after  
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36 204 adjusting for BMI (dyslipidemia with fast eating and hyperglycemia with slow eating in  
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39 205 men, and high blood pressure with slow eating in both men and women). Similarly, the  
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42 206 above-mentioned Korean study<sup>11</sup> reported that high rate of eating remained an important  
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45 207 determinant for low HDL-C and high fasting plasma glucose after adjustment for BMI  
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48 208 in men. Therefore, there may be pathways other than weight gain that might underlie the  
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51 209 association between eating rate and MetS.

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53 210 We found that the association between eating rate and MetS was stronger in  
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56 211 men than in women, consistent with a previous study in Korea.<sup>11</sup> Such sex difference  
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6 212 may reflect the difference in actual eating speed between men and women. One study  
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9 213 elucidated that women took more bites, smaller bite size and slower bites than men in  
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12 214 eating the same amount of doughnut, irrespectively of body size.<sup>26</sup> Another study  
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15 215 showed that objectively measured eating speed in men with self-reported slow eating  
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18 216 was faster than that in women with self-reported fast eating.<sup>27</sup> Taken together, eating  
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21 217 rate may have a greater impact on metabolism in men than that in women.

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23 218 Although mechanisms whereby eating rate influences metabolism is not fully  
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26 219 elucidated, overeating may link fast eating to MetS. Fast eating gives few satiety signal  
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29 220 from oral cavity to the brain,<sup>28, 29</sup> induces less satiation and satiety due to a lack of  
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32 221 stomach expansion<sup>30</sup> and alters the circulating levels of certain gut hormones.<sup>31, 32</sup> In  
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35 222 these pathways, fast eating leads to excess energy intake,<sup>33, 34</sup> resulting in overweight  
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38 223 and MetS. Because fast eating has been associated with obesity even after adjusting for  
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41 224 total energy intake,<sup>8-11, 14</sup> there may be other pathways. One study showed that  
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44 225 interleukin-1 $\beta$  and interleukin-6 were higher among those who ate fast than among  
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47 226 those who ate slowly, even after accounting for energy intake and BMI.<sup>35</sup> These  
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50 227 cytokines could induce insulin resistance,<sup>36, 37</sup> contributing to high blood pressure via an  
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53 228 increased renal sodium and water retention, plasma noradrenalin and sympathetic  
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56 229 nervous system activity.<sup>38-40</sup>

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6 230 The strengths of our study deserve mention. The present study has large sample  
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9 231 size (56,865 participants). In addition, body weight, body height and waist  
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12 232 circumference were measured by trained technicians, which increased the validity of our  
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15 233 study. Nonetheless, several limitations in the present study merit consideration. First,  
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18 234 eating rate was self-reported. However, self-reported eating rate has been shown to be  
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21 235 well correlated with friend-reported one<sup>9</sup> or objectively measured one.<sup>27</sup> Second, total  
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24 236 energy intake was not available in our study. However, because energy intake is  
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27 237 influenced by eating rate and thus may act as a mediator rather than confounder, the  
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30 238 adjustment of energy intake could underestimate the association between eating rate and  
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33 239 MetS. Moreover, eating rate has been associated with body weight independent of  
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36 240 energy intake.<sup>7-10, 13</sup> Third, the study participants were mainly workers in various  
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39 241 industries including manufacturing (43.6%), service (27.8%) and transport and  
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42 242 telecommunications (9.9%), and these figures are similar to those of national survey.<sup>41</sup>  
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45 243 However, information on profession of participants was not available, and thus caution  
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48 244 is required when generalize the present finding. Fourth, cross-sectional design precludes  
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51 245 any causal inferences about the role of eating rate. Finally, we cannot exclude a  
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54 246 possibility of the effects of residual confounding and confounding by unmeasured  
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57 247 variables.  
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6 248 In conclusion, we found a positive trend association between self-reported  
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9 249 eating rate and the presence of MetS in men and women. The association between  
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11 250 eating rate and MetS was largely accounted for by the difference of body mass across  
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15 251 eating rate. Further research should address whether reducing eating rate prevents  
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18 252 obesity and MetS.  
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Table 1. Characteristics of the study individuals according to eating rates

	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Age (years) <sup>b</sup>	46.9 ± 12.3	46.9 ± 10.9	45.0 ± 10.4	<0.001	43.5 ± 12.5	47.2 ± 11.6	46.7 ± 11.2	<0.001
Walking time, ≥60 min/day (%)	21.8	19.0	20.6	0.004	15.5	15.0	16.1	0.798
Smoking status (%)				<0.001				
Non-smoker	61.9	55.0	56.6		82.9	83.1	80.7	0.572



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7	Daily consuming <20 cigarettes							
8		28.6	34.6	31.3		16.0	15.7	17.6
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12	Daily consuming $\geq$ 20 cigarettes							
13		9.5	10.4	12.1		1.1	1.2	1.7
14	/day							
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18	Alcohol (%)							
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22					<0.00			<0.00
23	Non-drinker	30.2	26.7	26.7		53.4	52.2	49.8
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27	Drinker <1 go /day <sup>d</sup>	33.9	35.7	34.5		34.2	35.9	35.5
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30	Drinker 1 to <2 go /day <sup>d</sup>	24.6	26.3	26.8		9.5	9.5	11.5
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33	Drinker $\geq$ 2 go /day <sup>d</sup>	11.3	11.3	12.0		2.9	2.4	3.2
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36	BMI (kg/m <sup>2</sup> ) <sup>b</sup>	22.4 $\pm$ 3.3	23.4 $\pm$ 3.3	24.6 $\pm$ 3.7	<0.00	21.0 $\pm$ 3.5	21.8 $\pm$ 3.5	22.5 $\pm$ 3.8
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Waist circumference (cm) <sup>b</sup>	80.3 ± 9.2	82.9 ± 9.0	86.0 ± 9.8		75.5 ± 9.5	77.7 ± 9.4	79.6 ± 9.8	
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				<0.00				<0.00
Systolic blood pressure (mm Hg) <sup>b</sup>	123.5 ± 15.5	126.1 ± 15.5	126.7 ± 15.1		113.1 ± 16.3	117.3 ± 17.2	117.0 ± 17.2	
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				<0.00				<0.00
Diastolic blood pressure (mm Hg) <sup>b</sup>	75.2 ± 11.4	77.3 ± 11.9	78.0 ± 12.0		69.1 ± 10.9	71.4 ± 11.5	71.5 ± 11.9	
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					87 (82 to	88 (83 to		
Fasting plasma glucose (mg/dL) <sup>c</sup>	91 (85 to 98)	92 (86 to 99)	92 (86 to 99)	0.001	93)	94)	88 (83 to 94)	0.001
				<0.00	63 (48 to	69 (51 to	71 (52 to	<0.00
Triglyceride (mg/dL) <sup>c</sup>	92 (65 to	99 (69 to	107 (73 to 161)		87)	96)	101)	
	138)	148)		1				1

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				<0.00				<0.00
HDL-C (mg/dL) <sup>b</sup>	61.3 ± 15.3	59.4 ± 15.0	57.2 ± 14.3		71.4 ± 15.3	70.5 ± 15.8	69.3 ± 15.5	
				1				1

Cross to sectional survey of 56,865 examinees in All Japan Labor Welfare Foundation, Japan, 2011.

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Linear regression, an extension of the Wilcoxon Rank-Sum test and logistic regression, assigning ordinal number (0 to 2) to eating rate, as appropriate.

<sup>b</sup> Mean ± SD.

<sup>c</sup> medians (interquartile range).

<sup>d</sup> One *go* contains ~25g of ethanol.

Table 2. Odds ratios and 95% confidence intervals for metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
MetS, n	361	4,180	3,193		116	1,261	547	
Model 1 <sup>c</sup>	0.70 (0.62 to 0.79)	1.00	1.62 (1.53 to 1.71)	<0.001	0.75 (0.61 to 0.92)	1.00	1.27 (1.13 to 1.42)	<0.001
Model 2 <sup>d</sup>	0.70 (0.62 to 0.79)	1.00	1.61 (1.53 to 1.70)	<0.001	0.74 (0.60 to 0.91)	1.00	1.27 (1.13 to 1.43)	<0.001

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Model 3	0.91 (0.80 to	1.10 (1.03 to	<0.00	0.88 (0.70 to	0.98 (0.86 to	
	1.04)	1.17)	1	1.11)	1.12)	0.714
<sup>e</sup>						

MetS as defined using the criteria of the Joint Interim Statement : the presence of three or more of the following risk factors: 1) waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L).

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Adjusted for age.

<sup>d</sup> Adjusted for age, smoking status, alcohol, and regular physical activity.

<sup>e</sup> Adjusted for age, smoking status, alcohol, regular physical activity, and body mass index.

Table 3. Odds ratios and 95% confidence intervals for components of metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Central obesity <sup>c</sup>								
Model 1 <sup>d</sup>	0.63 (0.56 to 0.71)	1.00	1.98 (1.89 to 2.08)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.34 to 1.56)	<0.001
Model 2 <sup>e</sup>	0.63 (0.56 to 0.70)	1.00	1.97 (1.88 to 2.07)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.33 to 1.56)	<0.001

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High blood pressure <sup>f</sup>

Model 1 <sup>d</sup>	0.75 (0.69 to 0.82)	1.00	1.22 (1.17 to 1.27)	<0.001	0.76 (0.66 to 0.88)	1.00	1.10 (1.01 to 1.21)	<0.001
Model 2 <sup>e</sup>	0.74 (0.68 to 0.81)	1.00	1.20 (1.15 to 1.26)	<0.001	0.76 (0.65 to 0.88)	1.00	1.10 (1.00 to 1.20)	<0.001
Model 3 <sup>g</sup>	0.88 (0.81 to 0.96)	1.00	0.97 (0.93 to 1.02)	0.645	0.85 (0.72 to 0.99)	1.00	0.93 (0.84 to 1.02)	0.923

High fasting plasma glucose <sup>h</sup>

Model 1 <sup>d</sup>	0.78 (0.71 to 0.87)	1.00	1.17 (1.12 to 1.23)	<0.001	1.03 (0.85 to 1.25)	1.00	1.17 (1.04 to 1.31)	0.035
Model 2 <sup>e</sup>	0.78 (0.71 to 0.87)	1.00	1.16 (1.11 to 1.23)	<0.001	1.03 (0.85 to 1.25)	1.00	1.16 (1.03 to 1.31)	0.042

	0.87)		1.22)	1	1.25)		1.31)	
Model 3 <sup>g</sup>	0.88 (0.80 to	1.00	0.99 (0.94 to	0.238	1.14 (0.94 to	1.00	1.02 (0.90 to	0.536
	0.98)		1.05)		1.40)		1.15)	
High triglyceride <sup>i</sup>								
Model 1 <sup>d</sup>	0.88 (0.80 to	1.00	1.32 (1.26 to	<0.00	0.83 (0.67 to	1.00	1.14 (1.01 to	0.002
	0.96)		1.38)	1	1.01)		1.28)	
Model 2 <sup>e</sup>	0.90 (0.82 to	1.00	1.33 (1.27 to	<0.00	0.81 (0.66 to	1.00	1.13 (1.01 to	0.002
	0.98)		1.39)	1	1.00)		1.27)	
Model 3 <sup>g</sup>	1.08 (0.98 to	1.00	1.07 (1.02 to	0.121	0.90 (0.73 to	1.00	0.98 (0.87 to	0.753
	1.19)		1.12)		1.11)		1.11)	
Low HDL-C <sup>j</sup>								



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Model 1 <sup>c</sup>	0.83 (0.73 to 0.96)	1.00	1.34 (1.26 to 1.43)	<0.001	0.90 (0.74 to 1.09)	1.00	1.11 (0.99 to 1.25)	0.018
Model 2 <sup>d</sup>	0.83 (0.73 to 0.96)	1.00	1.36 (1.28 to 1.45)	<0.001	0.89 (0.74 to 1.08)	1.00	1.12 (1.00 to 1.26)	0.011
Model 3 <sup>e</sup>	0.97 (0.84 to 1.12)	1.00	1.10 (1.03 to 1.18)	0.004	1.00 (0.82 to 1.22)	1.00	0.96 (0.85 to 1.08)	0.500

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Waist circumference  $\geq 90$  cm in men,  $\geq 80$  cm in women.

<sup>d</sup> Adjusted for age.

<sup>e</sup> Adjusted for age, smoking status, alcohol, and regular physical activity.

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7 <sup>f</sup> Blood pressure  $\geq 130$  mm Hg for systolic or  $\geq 85$  mm Hg for diastolic.  
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10 <sup>g</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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13 <sup>h</sup> Fasting plasma glucose  $\geq 100$  mg/dL or under medication.  
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16 <sup>i</sup> Triglyceride  $\geq 150$  mg/dL or under medication.  
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19 <sup>j</sup> HDL-C  $< 40$  mg/dL in men,  $< 50$  mg/dL in women or under medication.  
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## Acknowledgments

The authors would like to thank Dr. Nobuo Yanagisawa and Dr. Takeshi Kawaguchi for their coordinating the study.

**Contributors:** SN and KKurotani designed study and drafted the manuscript. SN, NMP, AN, KKuwahara performed the data analysis. MD collected and interpreted the data. All authors have participated in the interpretation of the findings, revised it critically for important intellectual content and approved final version to be published. TM and YN provided administrative, technical and material support. SN and TM are guarantors.

**Funding:** This study was supported by the Industrial Health Foundation.

**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: all authors declare no interests.

**Ethical approval:** The research protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine and the Ethics Committee of Toho University.

**Data sharing:** No additional data available.

**Transparency:** SN affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant,

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For peer review only

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6 1 **Self-reported** eating rate and metabolic syndrome in Japanese: **cross-sectional**  
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9 2 **study**

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14 4 Satsue Nagahama <sup>1 2 3\*</sup>, Kayo Kurotani <sup>1</sup>, Ngoc Minh Pham <sup>4</sup>, Akiko Nanri <sup>1</sup>, Keisuke  
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45 46 Medicine and Pharmacy, Thai Nguyen Province, Vietnam;  
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52 17 Keywords: eating rate, metabolic syndrome, health checkup, Japan, **Joint Interim**  
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55 18 **Statement**  
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6 20 **ABSTRACT**  
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9 21 **Objectives:** To examine the association between self-reported eating rate and metabolic  
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12 22 syndrome.

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15 23 **Design:** Cross-sectional study.

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18 24 **Setting:** Annual health checkup at a health check service center in Japan.

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21 25 **Participants:** A total of 56,865 participants (41,820 males and 15,045 females) who  
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24 26 attended health checkup in 2011 and reported not to have a history of coronary heart  
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27 27 disease or stroke.

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29 28 **Main outcome measure:** Metabolic syndrome was defined by the joint of interim  
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32 29 statement of the International Diabetes Federation and the American Heart  
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35 30 Association/National Heart, Lung, and Blood Institute.

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38 31 **Results:** In multiple logistic regression models, eating rate was significantly and  
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41 32 positively associated with metabolic syndrome. The multivariable-adjusted odds ratios  
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44 33 (95% confidence interval) for slow, normal and fast were 0.70 (0.62 to 0.79), 1.00  
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47 34 (reference) and 1.61 (1.53 to 1.70), respectively, in men (P for trend <0.001), and 0.74  
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50 35 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
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53 36 trend <0.001). The association of eating rate and metabolic syndrome was attenuated  
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56 37 after further adjustment for body mass index in both sexes, but remained statistically

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6 38 significant in men. Of metabolic syndrome components, abdominal obesity showed the  
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9 39 strongest association with eating rate. The associations of slow eating with high blood  
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12 40 pressure and hyperglycemia and that of fast eating with lipid abnormality were still  
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15 41 significant in men, even after adjustment for body mass index.  
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18 42 **Conclusions:** Results suggest that eating rate is associated with the presence of  
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21 43 metabolic syndrome and that this association is largely accounted for by the difference  
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24 44 of body mass according to eating rate.  
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6 45 **Strength and Limitation**  
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9 46 This study included a large number of participants, used waist circumference in defining  
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12 47 metabolic syndrome, and analyzed data for men and women separately.  
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15 48 Eating rate was assessed by a self-reported questionnaire. Information on dietary intake  
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6 **50 Introduction**  
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9 51 Metabolic syndrome (MetS) is a cluster of physiological risk factors associated  
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11 52 with cardiovascular disease and several types of cancer.<sup>1</sup> Determination of etiologic  
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13 53 factors for MetS is required for the establishment of public health strategies to reduce its  
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15 54 prevalence and prevent resulting complications. Growing evidence from both  
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17 55 observational and interventional studies suggests a role of dietary habits in the  
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19 56 development of MetS,<sup>2-4</sup> which originates from obesity. Obesity has been extensively  
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21 57 investigated in relation to dietary habits including eating rate since 1962, when Ferster  
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23 58 published a theoretical and practical weight control program focusing on eating  
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25 59 behaviors including eating rate.<sup>5</sup> Observational studies showed that obese people ate at a  
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27 60 faster rate than non-obese people,<sup>6</sup> and reducing eating rate may be a simple and  
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29 61 effective therapy for obesity.<sup>7</sup>  
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41 62 During the past decade, several cross-sectional studies have found a positive  
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43 63 association between eating rate and overweight<sup>8-11</sup> or insulin resistance.<sup>11-15</sup> Similarly, a  
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45 64 few longitudinal studies showed that eating fast was associated with an increased risk of  
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47 65 weight gain<sup>16, 17</sup> and type 2 diabetes.<sup>18</sup> In addition, some cross-sectional studies have  
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49 66 reported that fast eating was positively associated with hypertriglyceridemia and low  
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51 67 high-density lipoprotein cholesterol (HDL-C).<sup>11, 14, 19</sup> Therefore it is conceivable that  
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6 68 eating rate may be associated with MetS. To our knowledge, however, only one Korean  
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9 69 study cross-sectionally examined eating rate in relation to MetS.<sup>20</sup> In that study, MetS  
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12 70 was defined by using body mass index (BMI), rather than waist circumference, and  
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15 71 investigated the association in men only. Waist circumference is a component of most  
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18 72 MetS definitions as a surrogate of central obesity, which can better predict  
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21 73 cardiovascular risk.<sup>21</sup> It is therefore necessary to examine the relationship between  
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24 74 eating rate and MetS using waist circumference in both sexes. Here, we investigated  
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27 75 cross-sectionally the association between self-reported eating rate and the presence of  
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30 76 MetS according to the joint of interim statement of the International Diabetes Federation  
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32 77 and the American Heart Association/National Heart, Lung, and Blood Institute (JIS)<sup>22</sup>  
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35 78 using a large dataset of health checkup in Japanese men and women.  
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## 41 **METHODS AND PROCEDURES**

### 42 43 44 **Study population**

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46 82 In Japan, health checkup under occupational health and safety law is mandatory  
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49 83 for all employed workers<sup>23</sup> and has been modified in 2008 when the recommendation  
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52 84 for new national health checkup system focusing on MetS has been launched.<sup>24</sup> Study  
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55 85 participants were attendants of 2011 (calendar year) annual health checkup at All Japan  
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6 86 Labor Welfare Foundation (Tokyo), a health service center performing health checkup.  
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9 87 Participants were mainly Japanese employees but also included a small number of their  
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12 88 dependents and foreign workers, aged 17-99 in men and 17-85 in women. Of 297,148  
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15 89 participants, we excluded 3,660 with a history of myocardial infarction, coronary heart  
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18 90 disease or stroke, 24,452 with missing information on eating rate, 192,581 who took  
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21 91 meal within 8 hours or provided no information on meal time, 204,423 with missing  
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24 92 data for any of the components of MetS, 15,886 with missing information on covariates  
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27 93 (BMI, smoking status, alcohol consumption and physical activity). Some participants  
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30 94 met more than one of these exclusion criteria, leaving 56,865 participants (41,820 males  
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32 95 and 15,045 females) for analysis. We did not obtain written informed consent from each  
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35 96 participant; instead, we disclosed the execution of the study by showing posters, giving  
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38 97 participants an opportunity to refuse the use of their data for the study. This procedure  
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41 98 conforms to the Japanese Ethical Guidelines for Epidemiological Research. The  
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44 99 research protocol was approved by the Ethics Committee of the National Center for  
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47 100 Global Health and Medicine and the Ethics Committee of Toho University.

#### 101 **Data collection and measurements**

102 A self-administered questionnaire, which was recommended for specific health  
103 examination by the Japanese government (Ministry of Health, Labour and Welfare),<sup>25</sup>

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6 104 was used to assess eating rate, medical history and health-related lifestyles including  
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9 105 smoking, alcohol consumption and regular physical activity. Eating rate was assessed by  
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12 106 asking “How fast is your speed of eating?”, with three response options (slow, normal  
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15 107 and fast). A trained staff measured height to the nearest 0.1 cm, weight to the nearest 0.1  
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18 108 kg and waist circumference to the nearest 0.1 cm at the umbilical level in a standing  
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21 109 position. BMI was calculated as the weight in kilograms divided by the squared height  
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24 110 in meters. Blood pressure in the sitting position was measured using an automated  
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27 111 machine (HEM-907, Omron, Kyoto, Japan). Participants with high blood pressure  
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30 112 ( $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic) received another measurement and data  
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33 113 showing lower systolic blood pressure was used. Venous blood sample was collected,  
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36 114 stored in a cooler at 4 degrees for transportation to an external laboratory (SRL, Tokyo,  
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39 115 Japan) and measured within 24 hours of blood drawing. Triglyceride level was  
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42 116 measured by enzymatic colorimetric test (Bio Majesty JCA-BM8060, JEOL, Tokyo,  
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45 117 Japan). HDL-C level was determined by a direct method (Bio Majesty JCA-BM8060,  
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48 118 JEOL, Tokyo, Japan). Plasma glucose levels were determined using by the hexokinase  
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51 119 method (an automatic clinical chemistry analyzer JCA-BM9000 series, JEOL, Tokyo,  
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54 120 Japan).

55 121 **Definitions for MetS**  
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6 122 According to the JIS criteria, MetS was defined as three or more of the  
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9 123 following risk factors: 1) waist circumference for Asian population  $\geq 90$  cm in men and  
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12 124  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$   
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15 125 mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood  
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18 126 pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$   
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21 127 mg/dL (5.6 mmol/L).<sup>22</sup> Participants under medication for diabetes, hypertension and  
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24 128 dyslipidemia were considered as having respective factor, irrespective of measured data.

### 129 **Statistical analysis**

130 Participants were divided into three groups according to eating rate (slow,  
131 normal and fast). The characteristics of participants across eating rate categories were  
132 expressed as means (standard deviation) for continuous variables and percentages for  
133 categorical variables, respectively. Fasting plasma glucose and triglyceride were  
134 expressed as medians (interquartile range) due to their skewed distribution. Trend  
135 association was assessed by assigning ordinal numbers (0 to 2) to the categories of  
136 eating rate (slow, normal and fast, respectively) and was tested using linear regression,  
137 an extension of the Wilcoxon Rank-Sum test and logistic regression, as appropriate.  
138 Multiple logistic regression analysis was used to estimate the odds ratios (OR) with  
139 95% confidence intervals (CI) for the presence of MetS across eating rate categories,

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6 140 with normal eating rate as the reference. We adjusted for age (continuous, year) in the  
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9 141 basic model. In the second model, we further adjusted for smoking status (non-smoker,  
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12 142 daily smoker consuming <20 cigarettes per day or  $\geq 20$  cigarettes per day), physical  
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15 143 activity (walking time <60 min per day or  $\geq 60$  min per day), and alcohol consumption  
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18 144 (non-drinker, <1 go, 1 to <2 go or  $\geq 2$  go per day; one go of sake, Japanese traditional  
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21 145 beverage, is about 180 ml of 10 to 14% of ethanol and contains ~23g of ethanol). In the  
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24 146 third model, we added BMI (continuous, kg/m<sup>2</sup>) to the second model. We performed  
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27 147 likelihood ratio test for testing the interaction between eating rate and sex. All analyses  
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30 148 were done for men and women separately because the interaction was significant (P for  
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33 149 interaction <0.001). We repeated the above analyses for each component of MetS.  
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36 150 Two-tailed P value <0.05 was considered statistically significant. All statistical analyses  
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39 151 were performed with STATA, version 12.1 (StataCorp, College Station, TX, USA).  
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## 43 153 RESULTS

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46 154 The prevalence of MetS was 18.5% in men and 12.9% in women. **Table 1**  
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49 155 shows characteristics of the study participants across categories of eating rate. Men who  
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52 156 ate fast tended to be young, whereas women who ate slowly tended to be young. Those  
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55 157 who ate fast had significantly higher BMI, waist circumference, triglyceride level and  
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6 158 systolic and diastolic blood pressures and lower HDL-C level in both men and women.  
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9 159 The ORs of the **presence** of MetS across eating rate are shown in **Table 2**.

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12 160 Faster eating was associated with higher **presence** of MetS in age- and

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15 161 multivariable-adjusted models. The trend was more apparent in men than in women.

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18 162 The multivariable-adjusted ORs (95% CI) of MetS for eating slow, normal and fast rate

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21 163 were 0.70 (0.62 to 0.79), 1.00 (reference) and 1.61 (1.53 to 1.70), respectively, in men

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24 164 (P for trend <0.001), and 0.74 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43),

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27 165 respectively, in women (P for trend <0.001). Further adjustment for BMI markedly

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30 166 attenuated these associations; however, the association with fast eating and MetS

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33 167 remained statistically significant in men.  
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35 168 **Table 3** shows the ORs of the **presence** of individual MetS components across

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38 169 three categories of eating rate. **The ORs of central obesity increased from slow to fast**

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41 170 eating in both men and women (OR 0.63, 1.00 (reference) and 1.97, respectively, in men

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44 171 (P for trend <0.001), and 0.73, 1.00(reference) and 1.44, respectively, in women (P for

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47 172 trend <0.001)). High blood pressure and **triglyceride** were positively associated with

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50 173 eating rate in both sexes. **High fasting plasma glucose and low HDL-C were associated**

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53 174 **with slow eating in both sexes, but they were associated with fast eating in men only.**

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56 175 Additional adjustment for BMI largely attenuated these associations, but the  
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6 176 associations of slow eating with high blood pressure (men and women) and  
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9 177 hyperglycemia (men) and those of fast eating with abnormal lipid profile (men)  
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12 178 remained statistically significant.

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## 16 17 18 180 **DISCUSSION**

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20 181 In this large population of Japanese men and women, we found that eating rate  
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23 182 was positively associated with the presence of MetS, especially in men. Of components  
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26 183 of MetS, the association with abdominal obesity was strongest. The relationship with  
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29 184 blood pressure in both sexes and fasting plasma glucose and lipids in men remained  
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32 185 statistically significant even after additional adjustment for BMI. To our best knowledge,  
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35 186 the present study is the first to report a positive association between eating rate and  
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38 187 MetS defined by using waist circumference.

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41 188 The present finding for MetS is consistent with that of a study among Korean  
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44 189 men reporting that eating rate was positively associated with MetS, which was defined  
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47 190 by using BMI instead of waist circumference.<sup>20</sup> As regards MetS components, our study  
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50 191 is compatible with some cross-sectional studies showing that eating rate was associated  
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53 192 with higher BMI<sup>8-10</sup> and two longitudinal studies showing that eating rate was  
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56 193 associated with weight gain.<sup>16, 17</sup> In a Korean study that elucidated the association  
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6 194 between eating rate and components of MetS for men and women separately, eating rate  
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9 195 was associated with obesity, high blood pressure, hyperglycemia and abnormal lipid  
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12 196 profile in men, whereas it was associated with only obesity in women.<sup>11</sup> Our results  
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15 197 were largely consistent with those in the Korean study (except for blood pressure in  
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18 198 women).

19 199 Notably, we found that the associations of MetS components with eating rate  
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23 200 were largely attenuated after adjustment for BMI, a finding compatible with those of a  
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26 201 cross-sectional study in Korea<sup>11</sup> and a prospective study in Japan.<sup>18</sup> This result indicates  
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29 202 that obesity is a mediator whereby fast eating deteriorates MetS components. We also  
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32 203 found, however, that some associations remained statistically significant even after  
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35 204 adjusting for BMI (dyslipidemia with fast eating and hyperglycemia with slow eating in  
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38 205 men, and high blood pressure with slow eating in both men and women). Similarly, the  
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41 206 above-mentioned Korean study<sup>11</sup> reported that high rate of eating remained an important  
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44 207 determinant for low HDL-C and high fasting plasma glucose after adjustment for BMI  
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47 208 in men. Therefore, there may be pathways other than weight gain that might underlie the  
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50 209 association between eating rate and MetS.

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53 210 We found that the association between eating rate and MetS was stronger in  
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56 211 men than in women, consistent with a previous study in Korea.<sup>11</sup> Such sex difference  
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6 212 may reflect the difference in actual eating speed between men and women. One study  
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9 213 elucidated that women took more bites, smaller bite size and slower bites than men in  
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12 214 eating the same amount of doughnut, irrespectively of body size.<sup>26</sup> Another study  
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15 215 showed that objectively measured eating speed in men with self-reported slow eating  
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18 216 was faster than that in women with self-reported fast eating.<sup>27</sup> Taken together, eating  
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21 217 rate may have a greater impact on metabolism in men than that in women.

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23 218 Although mechanisms whereby eating rate influences metabolism is not fully  
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26 219 elucidated, overeating may link fast eating to MetS. Fast eating gives few satiety signal  
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29 220 from oral cavity to the brain,<sup>28, 29</sup> induces less satiation and satiety due to a lack of  
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32 221 stomach expansion<sup>30</sup> and alters the circulating levels of certain gut hormones.<sup>31, 32</sup> In  
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35 222 these pathways, fast eating leads to excess energy intake,<sup>33, 34</sup> resulting in overweight  
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38 223 and MetS. Because fast eating has been associated with obesity even after adjusting for  
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41 224 total energy intake,<sup>8-11, 14</sup> there may be other pathways. One study showed that  
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44 225 interleukin-1 $\beta$  and interleukin-6 were higher among those who ate fast than among  
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47 226 those who ate slowly, even after accounting for energy intake and BMI.<sup>35</sup> These  
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50 227 cytokines could induce insulin resistance,<sup>36, 37</sup> contributing to high blood pressure via an  
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53 228 increased renal sodium and water retention, plasma noradrenalin and sympathetic  
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56 229 nervous system activity.<sup>38-40</sup>

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6 230 The strengths of our study deserve mention. The present study has large sample  
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9 231 size (56,865 participants). In addition, body weight, body height and waist  
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12 232 circumference were measured by trained technicians, which increased the validity of our  
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15 233 study. Nonetheless, several limitations in the present study merit consideration. First,  
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18 234 eating rate was self-reported. However, self-reported eating rate has been shown to be  
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21 235 well correlated with friend-reported one<sup>9</sup> or objectively measured one.<sup>27</sup> Second, total  
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24 236 energy intake was not available in our study. However, because energy intake is  
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27 237 influenced by eating rate and thus may act as a mediator rather than confounder, the  
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30 238 adjustment of energy intake could underestimate the association between eating rate and  
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33 239 MetS. Moreover, eating rate has been associated with body weight independent of  
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36 240 energy intake.<sup>7-10, 13</sup> Third, the study participants were mainly workers in various  
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39 241 industries including manufacturing (43.6%), service (27.8%) and transport and  
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42 242 telecommunications (9.9%), and these figures are similar to those of national survey.<sup>41</sup>  
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45 243 However, information on profession of participants was not available, and thus caution  
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48 244 is required when generalize the present finding. Fourth, cross-sectional design precludes  
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51 245 any causal inferences about the role of eating rate. Finally, we cannot exclude a  
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54 246 possibility of the effects of residual confounding and confounding by unmeasured  
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57 247 variables.  
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6 248 In conclusion, we found a positive trend association between self-reported  
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9 249 eating rate and the presence of MetS in men and women. The association between  
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11 250 eating rate and MetS was largely accounted for by the difference of body mass across  
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15 251 eating rate. Further research should address whether reducing eating rate prevents  
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18 252 obesity and MetS.  
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Table 1. Characteristics of the study individuals according to eating rates

	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Age (years) <sup>b</sup>	46.9 ± 12.3	46.9 ± 10.9	45.0 ± 10.4	<0.001	43.5 ± 12.5	47.2 ± 11.6	46.7 ± 11.2	<0.001
Walking time, ≥60 min/day (%)	21.8	19.0	20.6	0.004	15.5	15.0	16.1	0.798
Smoking status (%)				<0.001				
Non-smoker	61.9	55.0	56.6		82.9	83.1	80.7	0.572

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Daily consuming <20 cigarettes	28.6	34.6	31.3		16.0	15.7	17.6	
/day								
Daily consuming ≥20 cigarettes	9.5	10.4	12.1		1.1	1.2	1.7	
/day								
Alcohol (%)								
				<0.00				<0.00
Non-drinker	30.2	26.7	26.7		53.4	52.2	49.8	
				1				1
Drinker <1 go /day <sup>d</sup>	33.9	35.7	34.5		34.2	35.9	35.5	
Drinker 1 to <2 go /day <sup>d</sup>	24.6	26.3	26.8		9.5	9.5	11.5	
Drinker ≥2 go /day <sup>d</sup>	11.3	11.3	12.0		2.9	2.4	3.2	
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	22.4 ± 3.3	23.4 ± 3.3	24.6 ± 3.7	<0.00	21.0 ± 3.5	21.8 ± 3.5	22.5 ± 3.8	<0.00

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				<0.00				<0.00
Waist circumference (cm) <sup>b</sup>	80.3 ± 9.2	82.9 ± 9.0	86.0 ± 9.8		75.5 ± 9.5	77.7 ± 9.4	79.6 ± 9.8	
				1				1
				<0.00				<0.00
Systolic blood pressure (mm Hg) <sup>b</sup>	123.5 ± 15.5	126.1 ± 15.5	126.7 ± 15.1		113.1 ± 16.3	117.3 ± 17.2	117.0 ± 17.2	
				1				1
				<0.00				<0.00
Diastolic blood pressure (mm Hg) <sup>b</sup>	75.2 ± 11.4	77.3 ± 11.9	78.0 ± 12.0		69.1 ± 10.9	71.4 ± 11.5	71.5 ± 11.9	
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					87 (82 to	88 (83 to		
Fasting plasma glucose (mg/dL) <sup>c</sup>	91 (85 to 98)	92 (86 to 99)	92 (86 to 99)	0.001	93)	94)	88 (83 to 94)	0.001
				<0.00	63 (48 to	69 (51 to	71 (52 to	<0.00
Triglyceride (mg/dL) <sup>c</sup>	92 (65 to	99 (69 to	107 (73 to 161)		87)	96)	101)	
	138)	148)		1				1

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				<0.00				<0.00
HDL-C (mg/dL) <sup>b</sup>	61.3 ± 15.3	59.4 ± 15.0	57.2 ± 14.3		71.4 ± 15.3	70.5 ± 15.8	69.3 ± 15.5	
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Cross to sectional survey of 56,865 examinees in All Japan Labor Welfare Foundation, Japan, 2011.

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Linear regression, an extension of the Wilcoxon Rank-Sum test and logistic regression, assigning ordinal number (0 to 2) to eating rate, as appropriate.

<sup>b</sup> Mean ± SD.

<sup>c</sup> medians (interquartile range).

<sup>d</sup> One go contains ~25g of ethanol.

Table 2. Odds ratios and 95% confidence intervals for metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
MetS, n	361	4,180	3,193		116	1,261	547	
Model 1 <sup>c</sup>	0.70 (0.62 to 0.79)	1.00	1.62 (1.53 to 1.71)	<0.001	0.75 (0.61 to 0.92)	1.00	1.27 (1.13 to 1.42)	<0.001
Model 2 <sup>d</sup>	0.70 (0.62 to 0.79)	1.00	1.61 (1.53 to 1.70)	<0.001	0.74 (0.60 to 0.91)	1.00	1.27 (1.13 to 1.43)	<0.001



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Model 3	0.91 (0.80 to		1.10 (1.03 to	<0.00	0.88 (0.70 to		0.98 (0.86 to	
		1.00		1	1.11)	1.00		0.714
<sup>c</sup>	1.04)		1.17)				1.12)	

**MetS as defined using the criteria of the Joint Interim Statement** : the presence of three or more of the following risk factors: 1) waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L).

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Adjusted for age.

<sup>d</sup> Adjusted for age, smoking status, alcohol, and regular physical activity.

<sup>e</sup> Adjusted for age, smoking status, alcohol, regular physical activity, and body mass index.

Table 3. Odds ratios and 95% confidence intervals for components of metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Central obesity <sup>c</sup>								
Model 1 <sup>d</sup>	0.63 (0.56 to 0.71)	1.00	1.98 (1.89 to 2.08)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.34 to 1.56)	<0.001
Model 2 <sup>e</sup>	0.63 (0.56 to 0.70)	1.00	1.97 (1.88 to 2.07)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.33 to 1.56)	<0.001

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High blood pressure <sup>f</sup>

Model 1 <sup>d</sup>	0.75 (0.69 to 0.82)	1.00	1.22 (1.17 to 1.27)	<0.001	0.76 (0.66 to 0.88)	1.00	1.10 (1.01 to 1.21)	<0.001
Model 2 <sup>e</sup>	0.74 (0.68 to 0.81)	1.00	1.20 (1.15 to 1.26)	<0.001	0.76 (0.65 to 0.88)	1.00	1.10 (1.00 to 1.20)	<0.001
Model 3 <sup>g</sup>	0.88 (0.81 to 0.96)	1.00	0.97 (0.93 to 1.02)	0.645	0.85 (0.72 to 0.99)	1.00	0.93 (0.84 to 1.02)	0.923

High fasting plasma glucose <sup>h</sup>

Model 1 <sup>d</sup>	0.78 (0.71 to 0.87)	1.00	1.17 (1.12 to 1.23)	<0.001	1.03 (0.85 to 1.25)	1.00	1.17 (1.04 to 1.31)	0.035
Model 2 <sup>e</sup>	0.78 (0.71 to 0.87)	1.00	1.16 (1.11 to 1.23)	<0.001	1.03 (0.85 to 1.25)	1.00	1.16 (1.03 to 1.31)	0.042

	0.87)		1.22)	1	1.25)		1.31)	
Model 3 <sup>g</sup>	0.88 (0.80 to	1.00	0.99 (0.94 to	0.238	1.14 (0.94 to	1.00	1.02 (0.90 to	0.536
	0.98)		1.05)		1.40)		1.15)	
High triglyceride <sup>i</sup>								
Model 1 <sup>d</sup>	0.88 (0.80 to	1.00	1.32 (1.26 to	<0.00	0.83 (0.67 to	1.00	1.14 (1.01 to	0.002
	0.96)		1.38)	1	1.01)		1.28)	
Model 2 <sup>e</sup>	0.90 (0.82 to	1.00	1.33 (1.27 to	<0.00	0.81 (0.66 to	1.00	1.13 (1.01 to	0.002
	0.98)		1.39)	1	1.00)		1.27)	
Model 3 <sup>g</sup>	1.08 (0.98 to	1.00	1.07 (1.02 to	0.121	0.90 (0.73 to	1.00	0.98 (0.87 to	0.753
	1.19)		1.12)		1.11)		1.11)	
Low HDL-C <sup>j</sup>								

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Model 1 <sup>c</sup>	0.83 (0.73 to 0.96)	1.00	1.34 (1.26 to 1.43)	<0.001	0.90 (0.74 to 1.09)	1.00	1.11 (0.99 to 1.25)	0.018
Model 2 <sup>d</sup>	0.83 (0.73 to 0.96)	1.00	1.36 (1.28 to 1.45)	<0.001	0.89 (0.74 to 1.08)	1.00	1.12 (1.00 to 1.26)	0.011
Model 3 <sup>e</sup>	0.97 (0.84 to 1.12)	1.00	1.10 (1.03 to 1.18)	0.004	1.00 (0.82 to 1.22)	1.00	0.96 (0.85 to 1.08)	0.500

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Waist circumference  $\geq 90$  cm in men,  $\geq 80$  cm in women.

<sup>d</sup> Adjusted for age.

<sup>e</sup> Adjusted for age, smoking status, alcohol, and regular physical activity.

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7 <sup>f</sup> Blood pressure  $\geq 130$  mm Hg for systolic or  $\geq 85$  mm Hg for diastolic.  
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10 <sup>g</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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13 <sup>h</sup> Fasting plasma glucose  $\geq 100$  mg/dL or under medication.  
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16 <sup>i</sup> Triglyceride  $\geq 150$  mg/dL or under medication.  
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19 <sup>j</sup> HDL-C  $< 40$  mg/dL in men,  $< 50$  mg/dL in women or under medication.  
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## Acknowledgments

The authors would like to thank Dr. Nobuo Yanagisawa and Dr. Takeshi Kawaguchi for their coordinating the study.

Contributors: SN and KKurotani designed study and drafted the manuscript. SN, NMP, AN, KKuwahara performed the data analysis. MD collected and interpreted the data. All authors have participated in the interpretation of the findings, revised it critically for important intellectual content and approved final version to be published. TM and YN provided administrative, technical and material support. SN and TM are guarantors.

Funding: This study was supported by the Industrial Health Foundation.

Competing interests: All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: all authors declare no interests.

Ethical approval: The research protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine and the Ethics Committee of Toho University.

Data sharing: No additional data available.

Transparency: SN affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant,

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

MS ID#: bmjopen-2014-005241.R1

MS TITLE: Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional study

	Item No	Recommendation	Location in manuscript
<b>Title and abstract</b>	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	Line 1 on page 1 and line 23 on page 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	What was done: line 21-22 on page 3 What was found: line 42-44 on page 4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Scientific background: line 51-68 on page 6 and 7 Rationale: Line 68-74 on page 7
Objectives	3	State specific objectives, including any prespecified hypotheses	Line 74-78 on page 7
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	Line 75 on page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Line 84-88 on page 7-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Line 88-95 on page 8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Outcome: line 122-128 on page 10 Exposure: line 105-107 on page 9 Potential confounders: line 140-147 on page 11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Line 102-120 on page 8 and 9
Bias	9	Describe any efforts to address potential sources of bias	Exclusion: line 89-90 on page 8 Adjustment: line 140-147 on page 11
Study size	10	Explain how the study size was arrived at	Not provided
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Adjustment: line 140-147 on page 11

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Line 130-151 on page 10-11
		(b) Describe any methods used to examine subgroups and interactions	Line 146-149 on page 11
		(c) Explain how missing data were addressed	We excluded participants who had missing information on potential confounding variables (line 90 on page 8).
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Line 159-160 on page 11 Table 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 Line 154-178 on page 12 and 13
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	Table 2 Line 154 on page 11
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2, Table3 Line 159- on page 11-12
		(b) Report category boundaries when continuous variables were categorized	Table2, Table3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Line 147-149 on page 11
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	Line 181-185 on page 13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias	Line 233-247 on page 16



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or imprecision. Discuss both direction and magnitude of any potential bias

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Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Line 188-209 on page 13-14
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Generalisability	21	Discuss the generalisability (external validity) of the study results	Line 243-244 on page 16
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**Other information**

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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	This study was supported by the Industrial Health Foundation for drafting the manuscript.
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N/A: Not applicable.

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).

# BMJ Open

## Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2014-005241.R2
Article Type:	Research
Date Submitted by the Author:	31-Jul-2014
Complete List of Authors:	Nagahama, Satsue; All Japan Labor Welfare Foundation, ; School of Medicine, Toho University, Department of Environmental and Occupational Health Kurotani, Kayo; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Pham, Ngoc Minh; Thai Nguyen University of Medicine and Pharmacy, Department of Epidemiology, Faculty of Public Health Nanri, Akiko; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Kuwahara, Keisuke; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences Dan, Masashi; All Japan Labor Welfare Foundation, Department of Epidemiology and Prevention, Center for Clinical Sciences Nishiwaki, Yuji; School of Medicine, Toho University, Department of Environmental and Occupational Health Mizoue, Tetsuya; National Center for Global Health and Medicine, Department of Epidemiology and Prevention, Center for Clinical Sciences
<b>Primary Subject Heading</b>:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, PREVENTIVE MEDICINE, PUBLIC HEALTH

SCHOLARONE™  
Manuscripts

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6 1 **Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional**  
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9 2 **study**

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14 4 Satsue Nagahama <sup>1 2 3\*</sup>, Kayo Kurotani <sup>1</sup>, Ngoc Minh Pham <sup>4</sup>, Akiko Nanri <sup>1</sup>, Keisuke  
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52 17 Keywords: eating rate, metabolic syndrome, health checkup, Japan, Joint Interim  
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19 Word count: 2875

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6 20 **ABSTRACT**  
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9 21 **Objectives:** To examine the association between self-reported eating rate and metabolic  
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15 23 **Design:** Cross-sectional study.  
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18 24 **Setting:** Annual health checkup at a health check service center in Japan.  
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21 25 **Participants:** A total of 56,865 participants (41,820 males and 15,045 females) who  
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24 26 attended health checkup in 2011 and reported not to have a history of coronary heart  
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27 27 disease or stroke.  
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30 28 **Main outcome measure:** Metabolic syndrome was defined by the joint of interim  
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33 29 statement of the International Diabetes Federation and the American Heart  
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35 30 Association/National Heart, Lung, and Blood Institute.  
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38 31 **Results:** In multiple logistic regression models, eating rate was significantly and  
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41 32 positively associated with metabolic syndrome. The multivariable-adjusted odds ratios  
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44 33 (95% confidence interval) for slow, normal and fast were 0.70 (0.62 to 0.79), 1.00  
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47 34 (reference) and 1.61 (1.53 to 1.70), respectively, in men (P for trend <0.001), and 0.74  
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50 35 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
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53 36 trend <0.001). Of metabolic syndrome components, abdominal obesity showed the  
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56 37 strongest association with eating rate. The associations of eating rate and metabolic  
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6 38 syndrome and its components were largely attenuated after further adjustment for body  
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9 39 mass index; however, the association of slow eating with lower odds of high blood  
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12 40 pressure (men and women) and hyperglycemia (men) and that of fast eating with higher  
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15 41 odds of lipid abnormality (men) remained statistically significant.  
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17 42 **Conclusions:** Results suggest that eating rate is associated with the presence of  
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21 43 metabolic syndrome and that this association is largely accounted for by the difference  
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24 44 of body mass according to eating rate.  
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6 45 **Strength and Limitation**  
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9 46 This study included a large number of participants, used waist circumference in defining  
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12 47 metabolic syndrome, and analyzed data for men and women separately.

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15 48 Eating rate was assessed by a self-reported questionnaire. Information on dietary intake  
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6 **50 Introduction**  
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9 51 Metabolic syndrome (MetS) is a cluster of physiological risk factors associated  
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11 52 with cardiovascular disease and several types of cancer.<sup>1</sup> Determination of etiologic  
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13 53 factors for MetS is required for the establishment of public health strategies to reduce its  
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15 54 prevalence and prevent resulting complications. Growing evidence from both  
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17 55 observational and interventional studies suggests a role of dietary habits in the  
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19 56 development of MetS,<sup>2-4</sup> which originates from obesity. Obesity has been extensively  
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21 57 investigated in relation to dietary habits including eating rate since 1962, when Ferster  
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23 58 published a theoretical and practical weight control program focusing on eating  
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25 59 behaviors including eating rate.<sup>5</sup> Observational studies showed that obese people ate at a  
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27 60 faster rate than non-obese people,<sup>6</sup> and reducing eating rate may be a simple and  
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29 61 effective therapy for obesity.<sup>7</sup>  
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41 62 During the past decade, several cross-sectional studies have found a positive  
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43 63 association between eating rate and overweight<sup>8-11</sup> or insulin resistance.<sup>11-15</sup> Similarly, a  
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45 64 few longitudinal studies showed that eating fast was associated with an increased risk of  
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47 65 weight gain<sup>16, 17</sup> and type 2 diabetes.<sup>18</sup> In addition, some cross-sectional studies have  
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49 66 reported that fast eating was positively associated with hypertriglyceridemia and low  
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51 67 high-density lipoprotein cholesterol (HDL-C).<sup>11, 14, 19</sup> Therefore it is conceivable that  
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6 68 eating rate may be associated with MetS. To our knowledge, however, only one Korean  
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9 69 study cross-sectionally examined eating rate in relation to MetS.<sup>20</sup> In that study, MetS  
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12 70 was defined by using body mass index (BMI), rather than waist circumference, and  
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15 71 investigated the association in men only. Waist circumference is a component of most  
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18 72 MetS definitions as a surrogate of central obesity, which can better predict  
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21 73 cardiovascular risk.<sup>21</sup> It is therefore necessary to examine the relationship between  
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24 74 eating rate and MetS using waist circumference in both men and women. Here, we  
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27 75 investigated cross-sectionally the association between self-reported eating rate and the  
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30 76 presence of MetS according to the joint of interim statement of the International  
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33 77 Diabetes Federation and the American Heart Association/National Heart, Lung, and  
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36 78 Blood Institute (JIS)<sup>22</sup> using a large dataset of health checkup in Japanese men and  
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39 79 women.  
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## 43 44 81 **METHODS AND PROCEDURES**

### 45 46 47 82 **Study population**

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49 83 In Japan, health checkup under occupational health and safety law is mandatory  
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52 84 for all employed workers<sup>23</sup> and has been modified in 2008 when the recommendation  
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55 85 for new national health checkup system focusing on MetS has been launched.<sup>24</sup> Study  
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6 86 participants were attendants of 2011 (calendar year) annual health checkup at All Japan  
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9 87 Labor Welfare Foundation (Tokyo), a health service center performing health checkup.  
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12 88 Participants were mainly Japanese employees but also included a small number of their  
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15 89 dependents and foreign workers, aged 17-99 in men and 17-85 in women. Of 297,148  
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18 90 participants, we excluded 3,660 with a history of myocardial infarction, coronary heart  
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21 91 disease or stroke, which might influence both eating rate and MetS. Of the remaining  
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24 92 293,488 participants, we included 269,297 who reported their eating rate. Of these, we  
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27 93 excluded 182,487 with missing data for any of the components of MetS (173,376  
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30 94 without plasma glucose, 61,602 without waist circumference, 43,724 without  
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33 95 triglyceride, 43,401 without HDL-C and 504 without blood pressure; some participants  
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36 96 had two or more missing data). Major reason for a large number of participants with  
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39 97 missing measurement of blood glucose was that HbA1c was measured instead of blood  
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42 98 glucose for those who attended checkup in non-fasting condition. Of the remaining  
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45 99 86,810 participants, we further excluded 29,337 who took meal within 8 hours before  
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48 100 blood drawing or provided no information on meal time. After further exclusion of 608  
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51 101 participants with missing information on covariates (BMI, smoking status, alcohol  
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54 102 consumption and physical activity), 56,865 participants (41,820 males and 15,045  
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57 103 females) remained for analysis. We did not obtain written informed consent from each  
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6 104 participant; instead, we disclosed the execution of the study by showing posters, giving  
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9 105 participants an opportunity to refuse the use of their data for the study. In Japan,  
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12 106 informed consent is not necessarily required for observational studies using existing  
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15 107 data, as described in the Japanese Ethical Guidelines for Epidemiological Research.<sup>25</sup>  
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18 108 The research protocol was approved by the Ethics Committee of the National Center for  
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21 109 Global Health and Medicine and the Ethics Committee of Toho University.  
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### 23 110 **Data collection and measurements**

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26 111 A self-administered questionnaire, which was recommended for specific health  
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29 112 examination by the Japanese government (Ministry of Health, Labour and Welfare),<sup>26</sup>  
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32 113 was used to assess eating rate, medical history and health-related lifestyles including  
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35 114 smoking, alcohol consumption and regular physical activity. Eating rate was assessed by  
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38 115 asking “How fast is your speed of eating?”, with three response options (slow, normal  
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41 116 and fast). A trained staff measured height to the nearest 0.1 cm, weight to the nearest 0.1  
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44 117 kg and waist circumference to the nearest 0.1 cm at the umbilical level in a standing  
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47 118 position. BMI was calculated as the weight in kilograms divided by the squared height  
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50 119 in meters. Blood pressure in the sitting position was measured using an automated  
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53 120 machine (HEM-907, Omron, Kyoto, Japan). Participants with high blood pressure  
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56 121 ( $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic) received another measurement and data  
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6 122 showing lower systolic blood pressure was used. Venous blood sample was collected,  
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9 123 stored in a cooler at 4 degrees for transportation to an external laboratory (SRL, Tokyo,  
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12 124 Japan) and measured within 24 hours of blood drawing. Triglyceride level was  
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15 125 measured by enzymatic colorimetric test (Bio Majesty JCA-BM8060, JEOL, Tokyo,  
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18 126 Japan). HDL-C level was determined by a direct method (Bio Majesty JCA-BM8060,  
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21 127 JEOL, Tokyo, Japan). Plasma glucose level was determined using by the hexokinase  
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24 128 method (an automatic clinical chemistry analyzer JCA-BM9000 series, JEOL, Tokyo,  
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27 129 Japan).

### 130 **Definitions for MetS**

131 According to the JIS criteria, MetS was defined as three or more of the  
132 following risk factors: 1) waist circumference for Asian population  $\geq 90$  cm in men and  
133  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$   
134 mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood  
135 pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$   
136 mg/dL (5.6 mmol/L).<sup>22</sup> Participants under medication for diabetes, hypertension and  
137 dyslipidemia were considered as having respective factor, irrespective of measured data.

### 138 **Statistical analysis**

139 Participants were divided into three groups according to eating rate (slow,

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6 140 normal and fast). The characteristics of participants across eating rate categories were  
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9 141 expressed as means (standard deviation) for continuous variables and percentages for  
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12 142 categorical variables, respectively. Fasting plasma glucose and triglyceride were highly  
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15 143 skewed; hence, they were log-transformed and expressed as geometric means (95%  
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18 144 confidence intervals (CI)). Trend association was assessed by assigning ordinal numbers  
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21 145 (0 to 2) to the categories of eating rate (slow, normal and fast, respectively) and was  
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24 146 tested using linear regression and logistic regression, as appropriate. Multiple logistic  
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27 147 regression analysis was used to estimate the odds ratios (OR) with 95% CI for the  
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30 148 presence of MetS across eating rate categories, with normal eating rate as the reference.  
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32 149 We adjusted for age (continuous, year) in the basic model. In the second model, we  
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35 150 further adjusted for smoking status (non-smoker, daily smoker consuming <20  
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38 151 cigarettes per day or  $\geq 20$  cigarettes per day), physical activity (walking time <60 min  
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41 152 per day or  $\geq 60$  min per day), and alcohol consumption (non-drinker, <1 *go*, 1 to <2 *go*  
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44 153 or  $\geq 2$  *go* per day; one *go* of sake, Japanese traditional beverage, is about 180 ml of 10 to  
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47 154 14% of ethanol and contains  $\sim 23$ g of ethanol). In the third model, we added BMI  
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50 155 (continuous,  $\text{kg}/\text{m}^2$ ) to the second model. We performed likelihood ratio test for testing  
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53 156 the interaction between eating rate and sex. All analyses were done for men and women  
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56 157 separately because the interaction was significant (P for interaction <0.001). We  
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6 158 repeated the above analyses for each component of MetS. Two-tailed P value <0.05 was  
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9 159 considered statistically significant. All statistical analyses were performed with STATA,  
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12 160 version 12.1 (StataCorp, College Station, TX, USA).

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## 162 **RESULTS**

163 The prevalence of MetS was 18.5% in men and 12.8 % in women. **Table 1**  
164 shows characteristics of the study participants across categories of eating rate. Men who  
165 ate fast tended to be young, whereas women who ate slowly tended to be young. Both  
166 men and women who ate fast consumed greater amount of alcohol and had significantly  
167 higher BMI, waist circumference, triglyceride level and systolic and diastolic blood  
168 pressures and lower HDL-C level than those who ate slowly.

169 The ORs of the presence of MetS across eating rate are shown in **Table 2**.  
170 Faster eating was associated with higher presence of MetS in age- and  
171 multivariable-adjusted models. The trend was more apparent in men than in women.  
172 The multivariable-adjusted ORs (95% CI) of MetS for eating slow, normal and fast rate  
173 were 0.70 (0.62 to 0.79), 1.00 (reference) and 1.61 (1.53 to 1.70), respectively, in men  
174 (P for trend <0.001), and 0.74 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43),  
175 respectively, in women (P for trend <0.001). Further adjustment for BMI markedly

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6 176 attenuated these associations; however, the association with fast eating and MetS  
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9 177 remained statistically significant in men.

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11 **Table 3** shows the ORs of the presence of individual MetS components across  
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15 179 three categories of eating rate. Central obesity sharply increased with increasing speed  
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18 180 of eating; the ORs for slow, normal and fast eating were 0.63, 1.00 (reference) and 1.97,  
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21 181 respectively, in men (P for trend <0.001), and 0.73, 1.00(reference) and 1.44,  
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24 182 respectively, in women (P for trend <0.001). High blood pressure and high triglyceride  
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27 183 were positively associated with eating rate in both men and women. High fasting plasma  
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30 184 glucose and low HDL-C were associated with fast eating in both men and women, but  
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33 185 they were associated with slow eating in men only. Additional adjustment for BMI  
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36 186 largely attenuated these associations and the significant trend association disappeared,  
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39 187 but the associations of slow eating with decreased odds of high blood pressure (men and  
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42 188 women) and hyperglycemia (men) and those of fast eating with increased odds of  
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45 189 abnormal lipid profile (men) remained statistically significant.

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## 48 49 191 **DISCUSSION**

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52 192 In this large population of Japanese men and women, we found that eating rate  
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55 193 was positively associated with the presence of MetS, especially in men. Of components  
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6 194 of MetS, the association with abdominal obesity was strongest. These associations were  
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9 195 largely attenuated after adjustment for BMI. However, slow eating was associated with  
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12 196 decreased odds of high blood pressure in both men and women and high fasting plasma  
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15 197 glucose in men, and fast eating was associated with increased odds of lipid abnormal  
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18 198 profiles in men. To our best knowledge, the present study is the first to report a positive  
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21 199 association between eating rate and MetS defined by using waist circumference.  
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24 200 The present finding for MetS is consistent with that of a study among Korean  
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26 201 men reporting that eating rate was positively associated with MetS, which was defined  
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29 202 by using BMI instead of waist circumference.<sup>20</sup> As regards MetS components, our study  
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32 203 is compatible with some cross-sectional studies showing that eating rate was associated  
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35 204 with higher BMI<sup>8-11</sup> and two longitudinal studies showing that eating rate was  
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38 205 associated with weight gain.<sup>16, 17</sup> In a Korean study that elucidated the association  
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41 206 between eating rate and components of MetS for men and women separately, eating rate  
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44 207 was associated with obesity, high blood pressure, hyperglycemia and abnormal lipid  
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47 208 profile in men, whereas it was associated with only obesity in women.<sup>11</sup> Our results  
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50 209 were largely consistent with those in the Korean study (except for blood pressure in  
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53 210 women).  
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6 211 Notably, we found that the associations of MetS components with eating rate  
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9 212 were largely attenuated after adjustment for BMI, a finding compatible with those of a  
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12 213 cross-sectional study in Korea<sup>11</sup> and a prospective study in Japan.<sup>18</sup> This result indicates  
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15 214 that obesity is a mediator whereby fast eating deteriorates MetS components. We also  
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18 215 found, however, that some associations remained statistically significant even after  
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21 216 adjusting for BMI (dyslipidemia with fast eating and hyperglycemia with slow eating in  
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24 217 men, and high blood pressure with slow eating in both men and women). Similarly, the  
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27 218 above-mentioned Korean study<sup>11</sup> reported that high rate of eating remained an important  
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30 219 determinant for low HDL-C and high fasting plasma glucose after adjustment for BMI  
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33 220 in men. Therefore, there may be pathways other than weight gain that might underlie the  
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36 221 association between eating rate and MetS.

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38 222 We found that the association between eating rate and MetS was stronger in  
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41 223 men than in women, consistent with a previous study in Korea.<sup>11</sup> Such sex difference  
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44 224 may reflect the difference in actual eating speed between men and women. One study  
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47 225 elucidated that women took more bites, smaller bite size and slower bites than men in  
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50 226 eating the same amount of doughnut, irrespectively of body size.<sup>27</sup> Another study  
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53 227 showed that objectively measured eating speed in men with self-reported slow eating  
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6 228 was faster than that in women with self-reported fast eating.<sup>28</sup> Taken together, eating  
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9 229 rate may have a greater impact on metabolism in men than that in women.

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12 230 Although mechanisms whereby eating rate influences metabolism is not fully  
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15 231 elucidated, overeating may link fast eating to MetS. Fast eating gives few satiety signal  
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18 232 from oral cavity to the brain,<sup>29, 30</sup> induces less satiation and satiety due to a lack of  
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21 233 stomach expansion<sup>31</sup> and alters the circulating levels of certain gut hormones.<sup>32, 33</sup> In  
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24 234 these pathways, fast eating leads to excess energy intake,<sup>34, 35</sup> resulting in overweight  
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27 235 and MetS. Because fast eating has been associated with obesity even after adjusting for  
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30 236 total energy intake,<sup>8-11, 14</sup> there may be other pathways. One study showed that  
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33 237 interleukin-1 $\beta$  and interleukin-6 were higher among those who ate fast than among  
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36 238 those who ate slowly, even after accounting for energy intake and BMI.<sup>36</sup> These  
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39 239 cytokines could induce insulin resistance,<sup>37, 38</sup> contributing to high blood pressure via an  
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42 240 increased renal sodium and water retention, plasma noradrenalin and sympathetic  
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45 241 nervous system activity.<sup>39-41</sup>

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47 242 The strengths of our study deserve mention. The present study has large sample  
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50 243 size (56,865 participants). In addition, body weight, body height and waist  
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53 244 circumference were measured by trained technicians, which increased the validity of our  
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56 245 study. Nonetheless, several limitations in the present study merit consideration. First,

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6 246 eating rate was self-reported. However, self-reported eating rate has been shown to be  
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9 247 well correlated with friend-reported one<sup>9</sup> or objectively measured one.<sup>28</sup> Second,  
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12 248 information on dietary intake was not available in the present study and thus total  
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15 249 energy intake was not considered in analyses. The adjustment of energy intake, however,  
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18 250 may not be appropriate because energy intake may increase with eating rate and thus  
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21 251 may act as a mediator rather than confounder. Moreover, eating rate has been associated  
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24 252 with body weight independent of energy intake.<sup>7-10,13</sup> Third, fast-food is an energy-dense  
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27 253 dietary source and has been linked to MetS.<sup>42</sup> Because fast-food is usually consumed  
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30 254 quickly, it may confound the association of eating rate with MetS. Fourth, the study  
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33 255 participants were mainly workers in various industries including manufacturing (43.6%),  
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36 256 service (27.8%) and transport and telecommunications (9.9%), and these figures are  
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39 257 similar to those of national survey.<sup>43</sup> However, information on profession of participants  
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42 258 was not available, and thus caution is required when generalize the present finding.  
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45 259 Fifth, a large number of participants were excluded from the present analysis due to  
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48 260 missing data for MetS components. We cannot deny a possibility of bias due to such  
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51 261 selective inclusion. Sixth, cross-sectional design precludes any causal inferences about  
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54 262 the role of eating rate. Finally, we cannot exclude a possibility of the effects of residual  
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57 263 confounding and confounding by unmeasured variables.  
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6 264 In conclusion, we found a positive trend association between self-reported  
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9 265 eating rate and the presence of MetS in men and women. The association between  
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11 266 eating rate and MetS was largely accounted for by the difference of body mass across  
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14 267 eating rate. Further research should address whether reducing eating rate prevents  
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18 268 obesity and MetS.  
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Table 1. Characteristics of the study individuals according to eating rates

	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Age (years) <sup>b</sup>	46.9 ± 12.3	46.9 ± 10.9	45.0 ± 10.4	<0.001	43.5 ± 12.5	47.2 ± 11.6	46.7 ± 11.2	<0.001
Walking time, ≥60 min/day (%)	21.8	19.0	20.6	0.004	15.5	15.0	16.1	0.798
Smoking status (%)								
Non-smoker	61.9	55.0	56.6	<0.001	82.9	83.1	80.7	0.572
Daily consuming <20 cigarettes /day	28.6	34.6	31.3		16.0	15.7	17.6	
Daily consuming ≥20 cigarettes /day	9.5	10.4	12.1		1.1	1.2	1.7	

## Alcohol (%)

Non-drinker	30.2	26.7	26.7	<0.001	53.4	52.2	49.8	<0.001
Drinker <1 go /day <sup>d</sup>	33.9	35.7	34.5		34.2	35.9	35.5	
Drinker 1 to <2 go /day <sup>d</sup>	24.6	26.3	26.8		9.5	9.5	11.5	
Drinker ≥2 go /day <sup>d</sup>	11.3	11.3	12.0		2.9	2.4	3.2	
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	22.4 ± 3.3	23.4 ± 3.3	24.6 ± 3.7	<0.001	21.0 ± 3.5	21.8 ± 3.5	22.5 ± 3.8	<0.001
Waist circumference (cm) <sup>b</sup>	80.3 ± 9.2	82.9 ± 9.0	86.0 ± 9.8	<0.001	75.5 ± 9.5	77.7 ± 9.4	79.6 ± 9.8	<0.001
Systolic blood pressure (mm Hg) <sup>b</sup>	123.5 ± 15.5	126.1 ± 15.5	126.7 ± 15.1	<0.001	113.1 ± 16.3	117.3 ± 17.2	117.0 ± 17.2	<0.001
Diastolic blood pressure (mm Hg) <sup>b</sup>	75.2 ± 11.4	77.3 ± 11.9	78.0 ± 12.0	<0.001	69.1 ± 10.9	71.4 ± 11.5	71.5 ± 11.9	<0.001
Fasting plasma glucose (mg/dL) <sup>c</sup>	93.0 (92.5 to 93.6)	94.4 (94.2 to 94.6)	94.6 (94.3 to 94.8)	<0.001	88.1 (87.5 to 88.7)	89.1 (88.9 to 89.3)	89.5 (89.1 to 89.9)	<0.001

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Triglyceride (mg/dL) <sup>c</sup>	98.3 (96.2 to 103.8)	103.8 (103.0 to 110.8)	110.8 (109.8 to 111.9)	<0.001	67.0 (65.3 to 68.7)	71.6 (70.9 to 72.3)	74.1 (72.9 to 75.2)	<0.001
HDL-C (mg/dL) <sup>b</sup>	61.3 ± 15.3	59.4 ± 15.0	57.2 ± 14.3	<0.001	71.4 ± 15.3	70.5 ± 15.8	69.3 ± 15.5	<0.001

Cross to sectional survey of 56,865 examinees in All Japan Labor Welfare Foundation, Japan, 2011.

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Linear regression and logistic regression, assigning ordinal number (0 to 2) to eating rate, as appropriate.

<sup>b</sup> Mean ± SD.

<sup>c</sup> Geometric means (95% confidence intervals).

<sup>d</sup> One *go* contains ~25g of ethanol.

Table 2. Odds ratios and 95% confidence intervals for metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
MetS, n	361	4,180	3,193		116	1,261	547	
Model 1 <sup>c</sup>	0.70 (0.62 to 0.79)	1.00	1.62 (1.53 to 1.71)	<0.001	0.75 (0.61 to 0.92)	1.00	1.27 (1.13 to 1.42)	<0.001
Model 2 <sup>d</sup>	0.70 (0.62 to 0.79)	1.00	1.61 (1.53 to 1.70)	<0.001	0.74 (0.60 to 0.91)	1.00	1.27 (1.13 to 1.43)	<0.001
Model 3 <sup>e</sup>	0.91 (0.80 to 1.04)	1.00	1.10 (1.03 to 1.17)	<0.001	0.88 (0.70 to 1.11)	1.00	0.98 (0.86 to 1.12)	0.714

MetS=Metabolic syndrome.



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7 MetS as defined using the criteria of the Joint Interim Statement : the presence of three or more of the following risk factors: 1) waist circumference  $\geq 90$  cm  
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10 in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3  
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12 mmol/L) in women, 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L).  
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16 <sup>a</sup> Reference.

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19 <sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

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22 <sup>c</sup> Adjusted for age.

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25 <sup>d</sup> Adjusted for age, smoking status, alcohol and regular physical activity.

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28 <sup>e</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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Table 3. Odds ratios and 95% confidence intervals for components of metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Central obesity <sup>c</sup>								
Model 1 <sup>d</sup>	0.63 (0.56 to 0.71)	1.00	1.98 (1.89 to 2.08)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.34 to 1.56)	<0.001
Model 2 <sup>e</sup>	0.63 (0.56 to 0.70)	1.00	1.97 (1.88 to 2.07)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.33 to 1.56)	<0.001

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High blood pressure <sup>f</sup>

Model 1 <sup>d</sup>	0.75	(0.69 to 1.00)	1.22	(1.17 to 1.27)	<0.001	0.76	(0.66 to 1.00)	1.10	(1.01 to 1.21)	<0.001
Model 2 <sup>e</sup>	0.74	(0.68 to 1.00)	1.20	(1.15 to 1.26)	<0.001	0.76	(0.65 to 1.00)	1.10	(1.00 to 1.20)	<0.001
Model 3 <sup>g</sup>	0.88	(0.81 to 1.00)	0.97	(0.93 to 1.02)	0.645	0.85	(0.72 to 1.00)	0.93	(0.84 to 1.02)	0.923

High fasting plasma glucose <sup>h</sup>

Model 1 <sup>d</sup>	0.78	(0.71 to 1.00)	1.17	(1.12 to 1.23)	<0.001	1.03	(0.85 to 1.00)	1.17	(1.04 to 1.31)	0.035
Model 2 <sup>e</sup>	0.78	(0.71 to 1.00)	1.16	(1.11 to 1.23)	<0.001	1.03	(0.85 to 1.00)	1.16	(1.03 to 1.31)	0.042

	0.87)		1.22)	1	1.25)		1.31)
Model 3 <sup>g</sup>	0.88 (0.80 to 1.00)		0.99 (0.94 to 1.05)	0.238	1.14 (0.94 to 1.40)	1.00	1.02 (0.90 to 0.536)
High triglyceride <sup>i</sup>							
Model 1 <sup>d</sup>	0.88 (0.80 to 1.00)		1.32 (1.26 to 1.38)	<0.001	0.83 (0.67 to 1.01)	1.00	1.14 (1.01 to 0.002)
Model 2 <sup>e</sup>	0.90 (0.82 to 1.00)		1.33 (1.27 to 1.39)	<0.001	0.81 (0.66 to 1.00)	1.00	1.13 (1.01 to 0.002)
Model 3 <sup>g</sup>	1.08 (0.98 to 1.00)		1.07 (1.02 to 1.12)	0.121	0.90 (0.73 to 1.11)	1.00	0.98 (0.87 to 0.753)
Low HDL-C <sup>j</sup>							

Model 1 <sup>d</sup>	0.83 (0.73 to 1.00)	1.34 (1.26 to 1.43)	<0.001	0.90 (0.74 to 1.00)	1.11 (0.99 to 1.25)	0.018
Model 2 <sup>e</sup>	0.83 (0.73 to 1.00)	1.36 (1.28 to 1.45)	<0.001	0.89 (0.74 to 1.00)	1.12 (1.00 to 1.26)	0.011
Model 3 <sup>g</sup>	0.97 (0.84 to 1.00)	1.10 (1.03 to 1.18)	0.004	1.00 (0.82 to 1.22)	0.96 (0.85 to 1.08)	0.500

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women.

<sup>d</sup> Adjusted for age.

<sup>e</sup> Adjusted for age, smoking status, alcohol and regular physical activity.

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7 <sup>f</sup> Blood pressure  $\geq 130$  mm Hg for systolic or  $\geq 85$  mm Hg for diastolic.  
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10 <sup>g</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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13 <sup>h</sup> Fasting plasma glucose  $\geq 100$  mg/dL or under medication.  
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16 <sup>i</sup> Triglyceride  $\geq 150$  mg/dL or under medication.  
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19 <sup>j</sup> HDL-C  $< 40$  mg/dL in men,  $< 50$  mg/dL in women or under medication.  
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## Acknowledgments

The authors would like to thank Dr. Nobuo Yanagisawa and Dr. Takeshi Kawaguchi for their coordinating the study.

**Contributors:** SN and KKurotani designed study and drafted the manuscript. SN, NMP, AN, KKuwahara performed the data analysis. MD collected and interpreted the data. All authors have participated in the interpretation of the findings, revised it critically for important intellectual content and approved final version to be published. TM and YN provided administrative, technical and material support. SN and TM are guarantors.

**Funding:** This study was supported by the Industrial Health Foundation.

**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: all authors declare no interests.

**Ethical approval:** The research protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine and the Ethics Committee of Toho University.

**Data sharing:** No additional data available.

**Transparency:** SN affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant,

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6 1 **Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional**  
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20 **ABSTRACT**

21 **Objectives:** To examine the association between self-reported eating rate and metabolic  
22 syndrome.

23 **Design:** Cross-sectional study.

24 **Setting:** Annual health checkup at a health check service center in Japan.

25 **Participants:** A total of 56,865 participants (41,820 males and 15,045 females) who  
26 attended health checkup in 2011 and reported not to have a history of coronary heart  
27 disease or stroke.

28 **Main outcome measure:** Metabolic syndrome was defined by the joint of interim  
29 statement of the International Diabetes Federation and the American Heart  
30 Association/National Heart, Lung, and Blood Institute.

31 **Results:** In multiple logistic regression models, eating rate was significantly and  
32 positively associated with metabolic syndrome. The multivariable-adjusted odds ratios  
33 (95% confidence interval) for slow, normal and fast were 0.70 (0.62 to 0.79), 1.00  
34 (reference) and 1.61 (1.53 to 1.70), respectively, in men (P for trend <0.001), and 0.74  
35 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43), respectively, in women (P for  
36 trend <0.001). Of metabolic syndrome components, abdominal obesity showed the  
37 strongest association with eating rate. **The associations of eating rate and metabolic**

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6 38 syndrome and its components were largely attenuated after further adjustment for body  
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9 39 mass index; however, the association of slow eating with lower odds of high blood  
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12 40 pressure (men and women) and hyperglycemia (men) and that of fast eating with higher  
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15 41 odds of lipid abnormality (men) remained statistically significant.

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18 42 **Conclusions:** Results suggest that eating rate is associated with the presence of  
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21 43 metabolic syndrome and that this association is largely accounted for by the difference  
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24 44 of body mass according to eating rate.

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6 45 **Strength and Limitation**  
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9 46 This study included a large number of participants, used waist circumference in defining  
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12 47 metabolic syndrome, and analyzed data for men and women separately.  
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15 48 Eating rate was assessed by a self-reported questionnaire. Information on dietary intake  
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18 49 was not obtained.  
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6 **50 Introduction**  
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Metabolic syndrome (MetS) is a cluster of physiological risk factors associated with cardiovascular disease and several types of cancer.<sup>1</sup> Determination of etiologic factors for MetS is required for the establishment of public health strategies to reduce its prevalence and prevent resulting complications. Growing evidence from both observational and interventional studies suggests a role of dietary habits in the development of MetS,<sup>2-4</sup> which originates from obesity. Obesity has been extensively investigated in relation to dietary habits including eating rate since 1962, when Ferster published a theoretical and practical weight control program focusing on eating behaviors including eating rate.<sup>5</sup> Observational studies showed that obese people ate at a faster rate than non-obese people,<sup>6</sup> and reducing eating rate may be a simple and effective therapy for obesity.<sup>7</sup>

During the past decade, several cross-sectional studies have found a positive association between eating rate and overweight<sup>8-11</sup> or insulin resistance.<sup>11-15</sup> Similarly, a few longitudinal studies showed that eating fast was associated with an increased risk of weight gain<sup>16, 17</sup> and type 2 diabetes.<sup>18</sup> In addition, some cross-sectional studies have reported that fast eating was positively associated with hypertriglyceridemia and low high-density lipoprotein cholesterol (HDL-C).<sup>11, 14, 19</sup> Therefore it is conceivable that

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6 68 eating rate may be associated with MetS. To our knowledge, however, only one Korean  
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9 69 study cross-sectionally examined eating rate in relation to MetS.<sup>20</sup> In that study, MetS  
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12 70 was defined by using body mass index (BMI), rather than waist circumference, and  
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15 71 investigated the association in men only. Waist circumference is a component of most  
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18 72 MetS definitions as a surrogate of central obesity, which can better predict  
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21 73 cardiovascular risk.<sup>21</sup> It is therefore necessary to examine the relationship between  
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24 74 eating rate and MetS using waist circumference in both men and women. Here, we  
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27 75 investigated cross-sectionally the association between self-reported eating rate and the  
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30 76 presence of MetS according to the joint of interim statement of the International  
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33 77 Diabetes Federation and the American Heart Association/National Heart, Lung, and  
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36 78 Blood Institute (JIS)<sup>22</sup> using a large dataset of health checkup in Japanese men and  
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39 79 women.  
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## 43 44 81 **METHODS AND PROCEDURES**

### 45 46 47 82 **Study population**

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49 83 In Japan, health checkup under occupational health and safety law is mandatory  
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52 84 for all employed workers<sup>23</sup> and has been modified in 2008 when the recommendation  
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55 85 for new national health checkup system focusing on MetS has been launched.<sup>24</sup> Study  
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6 86 participants were attendants of 2011 (calendar year) annual health checkup at All Japan  
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9 87 Labor Welfare Foundation (Tokyo), a health service center performing health checkup.  
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12 88 Participants were mainly Japanese employees but also included a small number of their  
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15 89 dependents and foreign workers, aged 17-99 in men and 17-85 in women. Of 297,148  
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18 90 participants, we excluded 3,660 with a history of myocardial infarction, coronary heart  
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21 91 disease or stroke, which might influence both eating rate and MetS. Of the remaining  
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24 92 293,488 participants, we included 269,297 who reported their eating rate. Of these, we  
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27 93 excluded 182,487 with missing data for any of the components of MetS (173,376  
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30 94 without plasma glucose, 61,602 without waist circumference, 43,724 without  
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33 95 triglyceride, 43,401 without HDL-C and 504 without blood pressure; some participants  
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36 96 had two or more missing data). Major reason for a large number of participants with  
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39 97 missing measurement of blood glucose was that HbA1c was measured instead of blood  
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42 98 glucose for those who attended checkup in non-fasting condition. Of the remaining  
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45 99 86,810 participants, we further excluded 29,337 who took meal within 8 hours before  
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48 100 blood drawing or provided no information on meal time. After further exclusion of 608  
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51 101 participants with missing information on covariates (BMI, smoking status, alcohol  
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54 102 consumption and physical activity), 56,865 participants (41,820 males and 15,045  
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57 103 females) remained for analysis. We did not obtain written informed consent from each  
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6 104 participant; instead, we disclosed the execution of the study by showing posters, giving  
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9 105 participants an opportunity to refuse the use of their data for the study. In Japan,  
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12 106 informed consent is not necessarily required for observational studies using existing  
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15 107 data, as described in the Japanese Ethical Guidelines for Epidemiological Research.<sup>25</sup>  
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18 108 The research protocol was approved by the Ethics Committee of the National Center for  
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21 109 Global Health and Medicine and the Ethics Committee of Toho University.  
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### 23 110 **Data collection and measurements**

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26 111 A self-administered questionnaire, which was recommended for specific health  
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29 112 examination by the Japanese government (Ministry of Health, Labour and Welfare),<sup>26</sup>  
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32 113 was used to assess eating rate, medical history and health-related lifestyles including  
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35 114 smoking, alcohol consumption and regular physical activity. Eating rate was assessed by  
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38 115 asking “How fast is your speed of eating?”, with three response options (slow, normal  
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41 116 and fast). A trained staff measured height to the nearest 0.1 cm, weight to the nearest 0.1  
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44 117 kg and waist circumference to the nearest 0.1 cm at the umbilical level in a standing  
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47 118 position. BMI was calculated as the weight in kilograms divided by the squared height  
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50 119 in meters. Blood pressure in the sitting position was measured using an automated  
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53 120 machine (HEM-907, Omron, Kyoto, Japan). Participants with high blood pressure  
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56 121 ( $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic) received another measurement and data  
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6 122 showing lower systolic blood pressure was used. Venous blood sample was collected,  
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9 123 stored in a cooler at 4 degrees for transportation to an external laboratory (SRL, Tokyo,  
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12 124 Japan) and measured within 24 hours of blood drawing. Triglyceride level was  
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15 125 measured by enzymatic colorimetric test (Bio Majesty JCA-BM8060, JEOL, Tokyo,  
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18 126 Japan). HDL-C level was determined by a direct method (Bio Majesty JCA-BM8060,  
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21 127 JEOL, Tokyo, Japan). Plasma glucose level was determined using by the hexokinase  
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24 128 method (an automatic clinical chemistry analyzer JCA-BM9000 series, JEOL, Tokyo,  
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27 129 Japan).

### 130 **Definitions for MetS**

131 According to the JIS criteria, MetS was defined as three or more of the  
132 following risk factors: 1) waist circumference for Asian population  $\geq 90$  cm in men and  
133  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$   
134 mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3 mmol/L) in women, 4) blood  
135 pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$   
136 mg/dL (5.6 mmol/L).<sup>22</sup> Participants under medication for diabetes, hypertension and  
137 dyslipidemia were considered as having respective factor, irrespective of measured data.

### 138 **Statistical analysis**

139 Participants were divided into three groups according to eating rate (slow,

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6 140 normal and fast). The characteristics of participants across eating rate categories were  
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9 141 expressed as means (standard deviation) for continuous variables and percentages for  
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12 142 categorical variables, respectively. Fasting plasma glucose and triglyceride were highly  
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15 143 skewed; hence, they were log-transformed and expressed as geometric means (95%  
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18 144 confidence intervals (CI)). Trend association was assessed by assigning ordinal numbers  
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21 145 (0 to 2) to the categories of eating rate (slow, normal and fast, respectively) and was  
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24 146 tested using linear regression and logistic regression, as appropriate. Multiple logistic  
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27 147 regression analysis was used to estimate the odds ratios (OR) with 95% CI for the  
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30 148 presence of MetS across eating rate categories, with normal eating rate as the reference.  
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32 149 We adjusted for age (continuous, year) in the basic model. In the second model, we  
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35 150 further adjusted for smoking status (non-smoker, daily smoker consuming <20  
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38 151 cigarettes per day or  $\geq 20$  cigarettes per day), physical activity (walking time <60 min  
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41 152 per day or  $\geq 60$  min per day), and alcohol consumption (non-drinker, <1 go, 1 to <2 go  
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44 153 or  $\geq 2$  go per day; one go of sake, Japanese traditional beverage, is about 180 ml of 10 to  
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47 154 14% of ethanol and contains  $\sim 23$ g of ethanol). In the third model, we added BMI  
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50 155 (continuous,  $\text{kg}/\text{m}^2$ ) to the second model. We performed likelihood ratio test for testing  
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53 156 the interaction between eating rate and sex. All analyses were done for men and women  
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56 157 separately because the interaction was significant (P for interaction <0.001). We  
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6 158 repeated the above analyses for each component of MetS. Two-tailed P value <0.05 was  
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9 159 considered statistically significant. All statistical analyses were performed with STATA,  
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12 160 version 12.1 (StataCorp, College Station, TX, USA).

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## 162 **RESULTS**

163 The prevalence of MetS was 18.5% in men and 12.8 % in women. **Table 1**  
164 shows characteristics of the study participants across categories of eating rate. Men who  
165 ate fast tended to be young, whereas women who ate slowly tended to be young. **Both**  
166 **men and women who ate fast consumed greater amount of alcohol** and had significantly  
167 higher BMI, waist circumference, triglyceride level and systolic and diastolic blood  
168 pressures and lower HDL-C level **than those who ate slowly.**

169 The ORs of the presence of MetS across eating rate are shown in **Table 2.**  
170 Faster eating was associated with higher presence of MetS in age- and  
171 multivariable-adjusted models. The trend was more apparent in men than in women.  
172 The multivariable-adjusted ORs (95% CI) of MetS for eating slow, normal and fast rate  
173 were 0.70 (0.62 to 0.79), 1.00 (reference) and 1.61 (1.53 to 1.70), respectively, in men  
174 (P for trend <0.001), and 0.74 (0.60 to 0.91), 1.00 (reference) and 1.27 (1.13 to 1.43),  
175 respectively, in women (P for trend <0.001). Further adjustment for BMI markedly

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6 176 attenuated these associations; however, the association with fast eating and MetS  
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9 177 remained statistically significant in men.  
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11           **Table 3** shows the ORs of the presence of individual MetS components across  
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15 179 three categories of eating rate. **Central obesity sharply increased with increasing speed**  
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18 180 **of eating; the ORs for slow, normal and fast eating were** 0.63, 1.00 (reference) and 1.97,  
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21 181 respectively, in men (P for trend <0.001), and 0.73, 1.00(reference) and 1.44,  
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24 182 respectively, in women (P for trend <0.001). High blood pressure and **high** triglyceride  
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27 183 were positively associated with eating rate in both **men and women**. High fasting plasma  
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30 184 glucose and low HDL-C were associated with **fast** eating in both **men and women**, but  
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33 185 they were associated with **slow** eating in men only. Additional adjustment for BMI  
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36 186 largely attenuated these associations **and the significant trend association disappeared**,  
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39 187 but the associations of slow eating with **decreased odds** of high blood pressure (men and  
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42 188 women) and hyperglycemia (men) and those of fast eating with **increased odds of**  
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45 189 abnormal lipid profile (men) remained statistically significant.  
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## 48 49 191 **DISCUSSION**

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52 192           In this large population of Japanese men and women, we found that eating rate  
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55 193 was positively associated with the presence of MetS, especially in men. Of components  
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6 194 of MetS, the association with abdominal obesity was strongest. These associations were  
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9 195 largely attenuated after adjustment for BMI. However, slow eating was associated with  
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12 196 decreased odds of high blood pressure in both men and women and high fasting plasma  
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15 197 glucose in men, and fast eating was associated with increased odds of lipid abnormal  
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18 198 profiles in men. To our best knowledge, the present study is the first to report a positive  
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21 199 association between eating rate and MetS defined by using waist circumference.

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23 200 The present finding for MetS is consistent with that of a study among Korean  
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26 201 men reporting that eating rate was positively associated with MetS, which was defined  
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29 202 by using BMI instead of waist circumference.<sup>20</sup> As regards MetS components, our study  
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32 203 is compatible with some cross-sectional studies showing that eating rate was associated  
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35 204 with higher BMI<sup>8-11</sup> and two longitudinal studies showing that eating rate was  
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38 205 associated with weight gain.<sup>16, 17</sup> In a Korean study that elucidated the association  
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41 206 between eating rate and components of MetS for men and women separately, eating rate  
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44 207 was associated with obesity, high blood pressure, hyperglycemia and abnormal lipid  
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47 208 profile in men, whereas it was associated with only obesity in women.<sup>11</sup> Our results  
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50 209 were largely consistent with those in the Korean study (except for blood pressure in  
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53 210 women).

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6 211 Notably, we found that the associations of MetS components with eating rate  
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9 212 were largely attenuated after adjustment for BMI, a finding compatible with those of a  
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11 213 cross-sectional study in Korea<sup>11</sup> and a prospective study in Japan.<sup>18</sup> This result indicates  
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14 214 that obesity is a mediator whereby fast eating deteriorates MetS components. We also  
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17 215 found, however, that some associations remained statistically significant even after  
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20 216 adjusting for BMI (dyslipidemia with fast eating and hyperglycemia with slow eating in  
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23 217 men, and high blood pressure with slow eating in both men and women). Similarly, the  
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26 218 above-mentioned Korean study<sup>11</sup> reported that high rate of eating remained an important  
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29 219 determinant for low HDL-C and high fasting plasma glucose after adjustment for BMI  
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32 220 in men. Therefore, there may be pathways other than weight gain that might underlie the  
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35 221 association between eating rate and MetS.

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38 222 We found that the association between eating rate and MetS was stronger in  
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41 223 men than in women, consistent with a previous study in Korea.<sup>11</sup> Such sex difference  
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44 224 may reflect the difference in actual eating speed between men and women. One study  
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47 225 elucidated that women took more bites, smaller bite size and slower bites than men in  
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50 226 eating the same amount of doughnut, irrespectively of body size.<sup>27</sup> Another study  
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53 227 showed that objectively measured eating speed in men with self-reported slow eating  
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6 228 was faster than that in women with self-reported fast eating.<sup>28</sup> Taken together, eating  
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9 229 rate may have a greater impact on metabolism in men than that in women.

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12 230 Although mechanisms whereby eating rate influences metabolism is not fully  
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15 231 elucidated, overeating may link fast eating to MetS. Fast eating gives few satiety signal  
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18 232 from oral cavity to the brain,<sup>29, 30</sup> induces less satiation and satiety due to a lack of  
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21 233 stomach expansion<sup>31</sup> and alters the circulating levels of certain gut hormones.<sup>32, 33</sup> In  
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24 234 these pathways, fast eating leads to excess energy intake,<sup>34, 35</sup> resulting in overweight  
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27 235 and MetS. Because fast eating has been associated with obesity even after adjusting for  
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30 236 total energy intake,<sup>8-11, 14</sup> there may be other pathways. One study showed that  
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33 237 interleukin-1 $\beta$  and interleukin-6 were higher among those who ate fast than among  
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36 238 those who ate slowly, even after accounting for energy intake and BMI.<sup>36</sup> These  
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39 239 cytokines could induce insulin resistance,<sup>37, 38</sup> contributing to high blood pressure via an  
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42 240 increased renal sodium and water retention, plasma noradrenalin and sympathetic  
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45 241 nervous system activity.<sup>39-41</sup>

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47 242 The strengths of our study deserve mention. The present study has large sample  
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50 243 size (56,865 participants). In addition, body weight, body height and waist  
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53 244 circumference were measured by trained technicians, which increased the validity of our  
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56 245 study. Nonetheless, several limitations in the present study merit consideration. First,

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6 246 eating rate was self-reported. However, self-reported eating rate has been shown to be  
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9 247 well correlated with friend-reported one<sup>9</sup> or objectively measured one.<sup>28</sup> **Second,**  
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12 248 **information on dietary intake was not available in the present study and thus total**  
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15 249 **energy intake was not considered in analyses. The adjustment of energy intake, however,**  
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18 250 **may not be appropriate because energy intake may increase with eating rate and thus**  
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21 251 **may act as a mediator rather than confounder.** Moreover, eating rate has been associated  
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24 252 with body weight independent of energy intake.<sup>7-10,13</sup> **Third, fast-food is an energy-dense**  
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27 253 **dietary source and has been linked to MetS.<sup>42</sup> Because fast-food is usually consumed**  
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30 254 **quickly, it may confound the association of eating rate with MetS. Fourth, the study**  
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33 255 participants were mainly workers in various industries including manufacturing (43.6%),  
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36 256 service (27.8%) and transport and telecommunications (9.9%), and these figures are  
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39 257 similar to those of national survey.<sup>43</sup> However, information on profession of participants  
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42 258 was not available, and thus caution is required when generalize the present finding.  
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45 259 **Fifth, a large number of participants were excluded from the present analysis due to**  
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48 260 **missing data for MetS components. We cannot deny a possibility of bias due to such**  
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51 261 **selective inclusion. Sixth, cross-sectional design precludes any causal inferences about**  
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54 262 the role of eating rate. Finally, we cannot exclude a possibility of the effects of residual  
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57 263 confounding and confounding by unmeasured variables.  
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6 264 In conclusion, we found a positive trend association between self-reported  
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9 265 eating rate and the presence of MetS in men and women. The association between  
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11 266 eating rate and MetS was largely accounted for by the difference of body mass across  
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15 267 eating rate. Further research should address whether reducing eating rate prevents  
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18 268 obesity and MetS.  
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Table 1. Characteristics of the study individuals according to eating rates

	Men (n = 41,820)			P for trend <sup>a</sup>	Women (n = 15,045)			P for trend <sup>a</sup>
	Slow	Normal	Fast		Slow	Normal	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Age (years) <sup>b</sup>	46.9 ± 12.3	46.9 ± 10.9	45.0 ± 10.4	<0.001	43.5 ± 12.5	47.2 ± 11.6	46.7 ± 11.2	<0.001
Walking time, ≥60 min/day (%)	21.8	19.0	20.6	0.004	15.5	15.0	16.1	0.798
Smoking status (%)								
Non-smoker	61.9	55.0	56.6	<0.001	82.9	83.1	80.7	0.572
Daily consuming <20 cigarettes /day	28.6	34.6	31.3		16.0	15.7	17.6	
Daily consuming ≥20 cigarettes /day	9.5	10.4	12.1		1.1	1.2	1.7	

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Alcohol (%)									
Non-drinker	30.2	26.7	26.7	<0.001	53.4	52.2	49.8	<0.001	
Drinker <1 go /day <sup>d</sup>	33.9	35.7	34.5		34.2	35.9	35.5		
Drinker 1 to <2 go /day <sup>d</sup>	24.6	26.3	26.8		9.5	9.5	11.5		
Drinker ≥2 go /day <sup>d</sup>	11.3	11.3	12.0		2.9	2.4	3.2		
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	22.4 ± 3.3	23.4 ± 3.3	24.6 ± 3.7	<0.001	21.0 ± 3.5	21.8 ± 3.5	22.5 ± 3.8	<0.001	
Waist circumference (cm) <sup>b</sup>	80.3 ± 9.2	82.9 ± 9.0	86.0 ± 9.8	<0.001	75.5 ± 9.5	77.7 ± 9.4	79.6 ± 9.8	<0.001	
Systolic blood pressure (mm Hg) <sup>b</sup>	123.5 ± 15.5	126.1 ± 15.5	126.7 ± 15.1	<0.001	113.1 ± 16.3	117.3 ± 17.2	117.0 ± 17.2	<0.001	
Diastolic blood pressure (mm Hg) <sup>b</sup>	75.2 ± 11.4	77.3 ± 11.9	78.0 ± 12.0	<0.001	69.1 ± 10.9	71.4 ± 11.5	71.5 ± 11.9	<0.001	
Fasting plasma glucose (mg/dL) <sup>c</sup>	93.0 (92.5 to 93.6)	94.4 (94.2 to 94.6)	94.6 (94.3 to 94.8)	<0.001	88.1 (87.5 to 88.7)	89.1 (88.9 to 89.3)	89.5 (89.1 to 89.9)	<0.001	

Triglyceride (mg/dL) <sup>c</sup>	98.3 (96.2 to 103.8)	103.8 (103.0 to 110.8)	110.8 (109.8 to 111.9)	<0.001	67.0 (65.3 to 68.7)	71.6 (70.9 to 72.3)	74.1 (72.9 to 75.2)	<0.001
HDL-C (mg/dL) <sup>b</sup>	61.3 ± 15.3	59.4 ± 15.0	57.2 ± 14.3	<0.001	71.4 ± 15.3	70.5 ± 15.8	69.3 ± 15.5	<0.001

Cross to sectional survey of 56,865 examinees in All Japan Labor Welfare Foundation, Japan, 2011.

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Linear regression and logistic regression, assigning ordinal number (0 to 2) to eating rate, as appropriate.

<sup>b</sup> Mean ± SD.

<sup>c</sup> Geometric means (95% confidence intervals).

<sup>d</sup> One *go* contains ~25g of ethanol.

Table 2. Odds ratios and 95% confidence intervals for metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
MetS, n	361	4,180	3,193		116	1,261	547	
Model 1 <sup>c</sup>	0.70 (0.62 to 0.79)	1.00	1.62 (1.53 to 1.71)	<0.001	0.75 (0.61 to 0.92)	1.00	1.27 (1.13 to 1.42)	<0.001
Model 2 <sup>d</sup>	0.70 (0.62 to 0.79)	1.00	1.61 (1.53 to 1.70)	<0.001	0.74 (0.60 to 0.91)	1.00	1.27 (1.13 to 1.43)	<0.001
Model 3 <sup>e</sup>	0.91 (0.80 to 1.04)	1.00	1.10 (1.03 to 1.17)	<0.001	0.88 (0.70 to 1.11)	1.00	0.98 (0.86 to 1.12)	0.714

MetS=Metabolic syndrome.

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7 MetS as defined using the criteria of the Joint Interim Statement : the presence of three or more of the following risk factors: 1) waist circumference  $\geq 90$  cm  
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10 in men and  $\geq 80$  cm in women, 2) triglyceride level  $\geq 150$  mg/dL (1.7 mmol/L), 3) HDL-C level  $< 40$  mg/dL (1.04 mmol/L) in men and  $< 50$  mg/dL (1.3  
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12 mmol/L) in women, 4) blood pressure  $\geq 130$  mm Hg systolic or  $\geq 85$  mm Hg diastolic, 5) fasting glucose level  $\geq 100$  mg/dL (5.6 mmol/L).  
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16 <sup>a</sup> Reference.

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19 <sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

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22 <sup>c</sup> Adjusted for age.

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25 <sup>d</sup> Adjusted for age, smoking status, alcohol and regular physical activity.

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28 <sup>e</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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Table3. Odds ratios and 95% confidence intervals for components of metabolic syndrome according to eating rate (n = 56,865)

Eating rate	Men (n = 41,820)			P for trend <sup>b</sup>	Women (n = 15,045)			P for trend <sup>b</sup>
	Slow	Normal <sup>a</sup>	Fast		Slow	Normal <sup>a</sup>	Fast	
n (%)	2,821 (6.8)	24,893 (59.5)	14,106 (33.7)		1,398 (9.3)	9,893 (65.8)	3,754 (24.9)	
Central obesity <sup>c</sup>								
Model 1 <sup>d</sup>	0.63 (0.56 to 0.71)	1.00	1.98 (1.89 to 2.08)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.34 to 1.56)	<0.001
Model 2 <sup>e</sup>	0.63 (0.56 to 0.70)	1.00	1.97 (1.88 to 2.07)	<0.001	0.73 (0.64 to 0.83)	1.00	1.44 (1.33 to 1.56)	<0.001

High blood pressure <sup>f</sup>

Model 1 <sup>d</sup>	0.75 (0.69 to 1.00)	1.22 (1.17 to 1.27)	<0.001	0.76 (0.66 to 1.00)	1.10 (1.01 to 1.21)	<0.001
Model 2 <sup>e</sup>	0.74 (0.68 to 1.00)	1.20 (1.15 to 1.26)	<0.001	0.76 (0.65 to 1.00)	1.10 (1.00 to 1.20)	<0.001
Model 3 <sup>g</sup>	0.88 (0.81 to 1.00)	0.97 (0.93 to 1.02)	0.645	0.85 (0.72 to 1.00)	0.93 (0.84 to 1.02)	0.923

High fasting plasma glucose <sup>h</sup>

Model 1 <sup>d</sup>	0.78 (0.71 to 1.00)	1.17 (1.12 to 1.23)	<0.001	1.03 (0.85 to 1.00)	1.17 (1.04 to 1.31)	0.035
Model 2 <sup>e</sup>	0.78 (0.71 to 1.00)	1.16 (1.11 to 1.21)	<0.001	1.03 (0.85 to 1.00)	1.16 (1.03 to 1.29)	0.042



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	0.87)		1.22)	1	1.25)		1.31)
Model 3 <sup>g</sup>	0.88 (0.80 to		0.99 (0.94 to	0.238	1.14 (0.94 to		1.02 (0.90 to
	1.00		1.05)		1.40)	1.00	0.536
	0.98)		1.05)		1.40)		1.15)
High triglyceride <sup>i</sup>							
Model 1 <sup>d</sup>	0.88 (0.80 to		1.32 (1.26 to	<0.00	0.83 (0.67 to		1.14 (1.01 to
	1.00		1.38)	1	1.01)	1.00	0.002
	0.96)		1.38)	1	1.01)		1.28)
Model 2 <sup>e</sup>	0.90 (0.82 to		1.33 (1.27 to	<0.00	0.81 (0.66 to		1.13 (1.01 to
	1.00		1.39)	1	1.00)	1.00	0.002
	0.98)		1.39)	1	1.00)		1.27)
Model 3 <sup>g</sup>	1.08 (0.98 to		1.07 (1.02 to	0.121	0.90 (0.73 to		0.98 (0.87 to
	1.00		1.12)		1.11)	1.00	0.753
	1.19)		1.12)		1.11)		1.11)

Low HDL-C<sup>j</sup>

Model 1 <sup>d</sup>	0.83 (0.73 to 1.00)	1.34 (1.26 to 1.43)	<0.001	0.90 (0.74 to 1.00)	1.11 (0.99 to 1.25)	0.018
Model 2 <sup>e</sup>	0.83 (0.73 to 1.00)	1.36 (1.28 to 1.45)	<0.001	0.89 (0.74 to 1.00)	1.12 (1.00 to 1.26)	0.011
Model 3 <sup>g</sup>	0.97 (0.84 to 1.00)	1.10 (1.03 to 1.18)	0.004	1.00 (0.82 to 1.22)	0.96 (0.85 to 1.08)	0.500

BMI=body mass index; HDL-C=high to density lipoprotein cholesterol.

<sup>a</sup> Reference.

<sup>b</sup> Multiple logistic regression, assigning ordinal number (0 to 2) to eating rate.

<sup>c</sup> Waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women.

<sup>d</sup> Adjusted for age.

<sup>e</sup> Adjusted for age, smoking status, alcohol and regular physical activity.

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7 <sup>f</sup> Blood pressure  $\geq 130$  mm Hg for systolic or  $\geq 85$  mm Hg for diastolic.  
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10 <sup>g</sup> Adjusted for age, smoking status, alcohol, regular physical activity and body mass index.  
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13 <sup>h</sup> Fasting plasma glucose  $\geq 100$  mg/dL or under medication.  
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16 <sup>i</sup> Triglyceride  $\geq 150$  mg/dL or under medication.  
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19 <sup>j</sup> HDL-C  $< 40$  mg/dL in men,  $< 50$  mg/dL in women or under medication.  
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## Acknowledgments

The authors would like to thank Dr. Nobuo Yanagisawa and Dr. Takeshi Kawaguchi for their coordinating the study.

Contributors: SN and KKurotani designed study and drafted the manuscript. SN, NMP, AN, KKuwahara performed the data analysis. MD collected and interpreted the data. All authors have participated in the interpretation of the findings, revised it critically for important intellectual content and approved final version to be published. TM and YN provided administrative, technical and material support. SN and TM are guarantors.

Funding: This study was supported by the Industrial Health Foundation.

Competing interests: All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) and declare: all authors declare no interests.

Ethical approval: The research protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine and the Ethics Committee of Toho University.

Data sharing: No additional data available.

Transparency: SN affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant,

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Or peer review only

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

MS ID#: bmjopen-2014-005241.R1

MS TITLE: Self-reported eating rate and metabolic syndrome in Japanese: cross-sectional study

	Item No	Recommendation	Location in manuscript
<b>Title and abstract</b>	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	Line 1 on page 1 and line 23 on page 3
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	What was done: line 21-22 on page 3 What was found: line 42-44 on page 4
<b>Introduction</b>			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Scientific background: line 51-67 on page 6 Rationale: Line 67-74 on page 6 and 7
Objectives	3	State specific objectives, including any prespecified hypotheses	Line 73-79 on page 7
<b>Methods</b>			
Study design	4	Present key elements of study design early in the paper	Line 75 on page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Line 83-89 on page 7-8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	Line 89-103 on page 8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Outcome: line 131-138 on page 10 Exposure: line 115 on page 9 Potential confounders: line 149-155 on page 11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Line 116-129 on page 9 and 10
Bias	9	Describe any efforts to address potential sources of bias	Exclusion: line 89-103 on page 8 Adjustment: line 149-155 on page 11
Study size	10	Explain how the study size was arrived at	Not provided
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Adjustment: line 149-155 on page 11

Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	Line 140-157 on page 11
		(b) Describe any methods used to examine subgroups and interactions	Line 155-157 on page 11
		(c) Explain how missing data were addressed	We excluded participants who had missing information on potential confounding variables (line 100-102 on page 8).
		(d) If applicable, describe analytical methods taking account of sampling strategy	N/A
		(e) Describe any sensitivity analyses	N/A
<b>Results</b>			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Table 1
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1 Line 63-168 on page 12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	Table 2 Line 163 on page 12
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2, Table3 Line 169-189 on page 12-13
		(b) Report category boundaries when continuous variables were categorized	Table2, Table3
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Line 155-156 on page 11
<b>Discussion</b>			
Key results	18	Summarise key results with reference to study objectives	Line 192-199 on page 13 and 14
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias	Line 245-263 on page 16 and 17

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or imprecision. Discuss both direction and magnitude of any potential bias

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Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Line 200-210 on page 14
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Generalisability	21	Discuss the generalisability (external validity) of the study results	Line 254-258 on page 17
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**Other information**

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Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	This study was supported by the Industrial Health Foundation for drafting the manuscript.
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N/A: Not applicable.

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).