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Original Article

Association between awareness of limiting food intake and allcause mortality: A cohort study in Japan

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1 ABSTRACT

2 **Background:** Improving diets requires an awareness of the need to limit foods for which excessive consumption is a health problem. Since there are limited reports on the link 3 between this awareness and mortality risk, we examined the association between 4 awareness of limiting food intake (energy, fat, and sweets) and all-cause mortality in a 5 6 Japanese cohort study. 7 Methods: Participants comprised 58,772 residents (27,294 men; 31,478 women) aged 35-69 years who completed baseline surveys of the Japan Multi-Institutional 8 9 Collaborative Cohort Study from 2004 to 2014. Hazard ratios (HRs) for all-cause 10 mortality and 95% confidence intervals (CIs) were estimated by sex using a Cox 11 proportional hazard model, with adjustment for related factors. Mediation analysis with 12 fat intake as a mediator was also conducted. 13 Results: The mean follow-up period was 11 years and 2,516 people died. Estimated 14 energy and fat intakes according to the Food Frequency Questionnaire were lower in those 15 with awareness of limiting food intake than in those without this awareness. Women with 16 awareness of limiting fat intake showed a significant decrease in mortality risk (HR=0.73; 17 95% CI, 0.55 to 0.94). Mediation analysis revealed that this association was due to the 18 direct effect of the awareness of limiting fat intake and that the total effect was not

- 19 mediated by actual fat intake. Awareness of limiting energy or sweets intake was not
- 20 related to mortality risk reduction.
- 21 Conclusion: Awareness of limiting food intake had a limited effect on reducing all-cause
- 22 mortality risk.
- 23 Keywords: awareness of limiting food intake, all-cause mortality, cohort study
- 24

25 INTRODUCTION

26 In 2017, an estimated 11 million people died worldwide due to noncommunicable 27 diseases; 29% of these deaths were due to diet, in which, fat and sugar-containing beverage unbalanced intake played a major role.¹ Furthermore, overeating is one of the 28 causes of noncommunicable diseases, and an excessive intake of energy, fat, and sweets 29 is associated with mortality risk.²⁻⁴ Therefore, the prevention of overeating and relevant 30 31 dietary behavior changes are important. Awareness is the first stage of behavioral changes. Prochaska et al. proposed a 32 33 behavioral change stage model, wherein awareness transforms into behaviors (Transtheoretical Model), with five stages in the health transformation process: 34 35 precontemplation, contemplation, preparation, action, and maintenance.⁵ The 36 Transtheoretical Model has been used as a framework in interventions for smoking cessation,^{6,7} as well as diet^{8,9} and exercise.^{10,11} Furthermore, numerous efforts have 37 38 focused on increasing awareness of limiting foods for which overconsumption is a health problem. For example, in the United States, calorie labeling has been stipulated by law 39 40 since 2018, with an estimated savings of \$260 million over a 6-year period (from 2018 to 2023) compared to conventional medical expenses.¹² Furthermore, a meta-analysis 41 reported energy and fat intake as negatively associated with calorie and nutrient content 42

43 labeling.¹³ Similar labeling has also resulted in a reduction in the purchase of sugar44 containing beverages,¹⁴ and, in some subgroups, has resulted in reduced energy intake,
45 medical costs, and body weight.¹⁵ Awareness of food intake restrictions may help prevent
46 overeating.

Awareness of limiting food intake will mediate food intake and be associated with 47 death as an independent factor, similar to noncommunicable diseases, exercise,¹⁶ and 48 smoking.¹⁷ Although studies on the association between awareness of limiting foods for 49 which overconsumption is a health problem and dietary behaviors have been reported, 50 studies on the association between such awareness and the risk of death, as well as on 51 52 factors that mediate this causation, is limited. Therefore, we evaluated the association 53 between awareness of limiting intake of energy, fat, and sweets and all-cause mortality in a Japanese cohort. Our hypothesis is that individuals with awareness of limiting food 54 intake (energy, fat, and sweets) are less likely to overeat and consequently have lower 55 56 mortality.

57

58 METHODS

59 Participants

8

60	This study used data from the Japan Multi-Institutional Collaborative Cohort (J-MICC)
61	Study. Details of the J-MICC study are available elsewhere. ¹⁸⁻²⁰ Briefly, the J-MICC
62	study is a molecular epidemiological study aimed at preventing lifestyle-related diseases
63	in Japanese people. In this study, residents in the community, health checkup examinees,
64	and first-visit patients at a cancer hospital were recruited. Baseline surveys were
65	conducted from 2004 to 2014, and were completed by 92,525 Japanese adults aged 35-
66	69 years (dataset 20220809). The target regions were Chiba, Shizuoka, Aichi, Mie, Shiga,
67	Kyoto, Tokushima, Fukuoka, Saga, Nagasaki, Kagoshima, and Okinawa. Those who
68	submitted written informed consent were selected as research participants.
69	Of the 92,525 participants in the J-MICC Study, 59,682 had available data on
70	awareness of limiting intake of energy, fat, and sweets, food intake, blood pressure, serum
71	lipid levels, fasting blood glucose or HbA1c levels, and history of treatment for
72	hypertension, dyslipidemia, or diabetes. As result, all participants from Chiba were
73	excluded. We further excluded those with no follow-up data (N=38), those who died
74	within 1 year of follow-up (N=76), and those with daily energy intake <1,000 kcal or
75	>4,000 kcal (N=796). Finally, 58,772 people (27,294 men and 31,478 women) were
76	included in the analysis.

This study was conducted in accordance with the Declaration of Helsinki, and the study
protocol was approved by the ethics review board of all institutions and universities
participating in the J-MICC Study.

80

81 Medical examination data

We collected information on the results of medical examinations and complete-health
checkups. In regions without linked medical examinations, medical examination items
were measured independently. Medical examination items included height, weight, body
mass index (BMI), systolic and diastolic blood pressures, serum levels of triglyceride and
high-density lipoprotein cholesterol, fasting blood glucose level, HbA1c level, and other
blood/biochemical test results.
Dyslipidemia was defined as a triglyceride level ≥150 mmHg/dL, high-density

Dyslipidemia was defined as a triglyceride level ≥150 mmHg/dL, high-density
lipoprotein cholesterol level <40 mg/dL, or the use of dyslipidemia medication.
Hypertension was defined as systolic blood pressure ≥130 mmHg, diastolic blood
pressure ≥85 mmHg, or the use of antihypertensive medication. Glucose intolerance was
defined as a fasting blood glucose level ≥100 mg/dL, HbA1c level ≥5.6%, or the use of
anti-diabetic medication. Obesity was defined as BMI ≥25 kg/m².²¹

94

95 Questionnaire surveys

96 Baseline surveys included a common questionnaire that collected information on sleep, 97 exercise, alcohol drinking habits, smoking habits, psychological stress, use of medications and supplements, dietary habits (including food intake), and medical 98 99 histories including those of family members (and a reproductive history in women). 100 To assess awareness of limiting food intake, participants were asked whether they avoid 101 consumption of energy, fat, or sweets, with "yes" or "no" as responses. Those who 102 answered "yes" were deemed to have awareness, indicating the subjective recognition for 103 the restriction of food intake, rather than actual food restriction. 104 Furthermore, those who indicated that they have a habit of drinking alcoholic beverages 105 at least once a month were regarded as "current drinkers," and those who indicated that 106 they were currently smoking were regarded as "current smokers." The amount of habitual exercise was estimated by a method similar to the International Physical Activity 107 Questionnaire (IPAQ).²² Habitual exercise was classified into three categories and 108 109 assigned an exercise intensity as follows: "walking", 3.3 METs; "moderate activity", 4.0 METs; and "vigorous activity", 8.0 METs. Metabolic equivalent of task values were 110 111 calculated by multiplying the assigned intensity by the frequency and duration of each 112 category. Additionally, daily activities were quantified by multiplying the duration of

"force work," "walking," "standing," and "sitting" with respective activity intensity values,
4.5, 3.0, 2.0, and 1.5 METs.²³ The participants were divided into tertiles according the
distribution of habitual exercise and daily activity.

116

117 Energy and nutrient intake

118 Daily intake of energy (kcal) and fat (gram) was estimated using the Food Frequency 119 Questionnaire (FFQ). Briefly, information on the dietary habits of the past year was 120 collected, including the frequency of intake of 47 staples, foods, and beverages, and the 121 amount of staple foods consumed for breakfast, lunch, and dinner. Estimated values for energy and fat intake on the FFQ have been validated by weighted diet records,²⁴⁻²⁶ 122 123 Validity indices for energy estimates in males and females were reported as 0.40 and 0.44, respectively, and those for fat were reported as 0.62 and 0.48, respectively.²⁴⁻²⁶ For sweet 124 foods, only frequency information was collected by the FFQ; accordingly, sugar intake 125 126 could not be evaluated as a nutrient. Therefore, in the current study, sweet food was 127 defined as cake and Japanese cake. The frequency of intake of cake and Japanese cake, 128 beef and pork, green and yellow vegetables, and fruits were calculated as weekly averages, 129 based on an 8-point scale (almost never eat, 1-3 times per month, 1-2 times per week, 3-130 4 times per week, 5-6 times per week, once per day, twice per day, and >3 times per day).

131 Tertiles were created for each intake of beef and pork, green and yellow vegetables, and132 fruits for men and women and were used for statistical analysis.

133

134 Follow-up and mortality data

135 Participants were followed up from the start of baseline survey, and the final year of the 136 follow-up varied from the end of 2017 to the end of 2020, depending on the study area. 137 Participants who moved out of study regions were censored. The duration of follow-up 138 was calculated as the time from the date of the participant's baseline survey to their death, 139 move out of study regions, or end of the follow-up, whichever came first. During an 140 average follow-up of 11 years (range: 0–15.9 years), 2,516 people died, and 3,154 people 141 moved out of study regions. The information on death was confirmed by death certificates 142 at the applicable health center, with the permission of the Japanese Ministry of Health, 143 Labor and Welfare.

144

145 Statistical analysis

The associations between awareness of limiting food intake and nutritional intake
estimated by the FFQ were determined according to sex using multivariable regression
analyses. Age, BMI, region, smoking and alcohol drinking habits, years of education,

149	daily activity, and habitual exercise were used as covariates. In the analyses for the
150	association with fat intake, the effect of estimated energy intake was additionally adjusted.
151	The distributions of age, BMI, and awareness of limiting food intake, but excluding
152	that used as a dependent variable, were compared by awareness of limiting food intake
153	using logistic regression models, and age was always included in the model (eTables).
154	Cox proportional hazards modeling was used to evaluate the association between
155	awareness of limiting food intake and mortality one year after the baseline survey; the
156	hazard ratio (HR) and 95% confidence interval (CI) were calculated by sex. To infer
157	causal relationships, we selected the covariates for the multivariate analysis based on
158	lifestyle-related factors pertaining to metabolic syndrome diagnostic criteria and factors
159	that would affect the association between awareness of limiting food intake and all-cause
160	mortality, and these covariates were evaluated through drawing Direct Acyclic Graphs
161	(DAG) (DAGitty3.0, http://www.dagitty.net/), and confirmed the effect by adjustment
162	(total effect) for causal effect identification. The following factors were applied in the
163	DAG: age (35-49, 50-59, and 60-69 years), BMI (<18.5, 18.5-24.9, and ≥25.0), 11 study
164	regions, smoking status (current, past, and never), alcohol drinking habit (current, past,
165	and never), years of education (<16 and \geq 16 years), daily activity (tertile), habitual
166	exercise (tertile), beef and pork intake (tertile), green and yellow vegetable intake (tertile),

167	fruit intake (tertile), awareness of energy intake, awareness of limiting fat intake,
168	awareness of limiting sweets intake, energy intake (continuous variable), fat intake
169	(continuous variable), sweets intake (the more frequent intake value of either cake or
170	Japanese cake), and the presence of dyslipidemia, hypertension, and glucose intolerance.
171	For statistical models, we used variables that did not have a biasing path in the DAG
172	(eFigure 1, 2, and 3).
173	The main causes of death in the study population were cancer and cerebrovascular
174	disease, and metabolic syndrome is an important high-risk condition for these diseases.
175	In general, individuals with metabolic syndrome are likely to have greater awareness of
176	limiting food intake because of the need to manage these underlying diseases. To exclude
177	the effects of causal reversals, subclass analyses were performed with stratification by
178	referring to diagnostic criteria for metabolic syndrome: central obesity, dyslipidemia,
179	hypertension, and hyperglycemia. Awareness of limiting energy intake was stratified by
180	BMI, fat intake was stratified by dyslipidemia and BMI, and sweets intake was stratified
181	by glucose intolerance and BMI.
182	In addition, we conducted a mediation analysis using the four-way effect
183	decomposition to evaluate the association between fat intake, as a mediator of awareness

184 of limiting fat intake, and all-cause mortality. This analysis can estimate the four-way

185	decomposition of controlled direct effect, reference interaction (only interaction),
186	mediated interaction, and pure indirect effect (only mediation). The exposure was
187	awareness of limiting fat intake, and the mediator was fat intake (continuous variable).
188	The average value of fat intake without awareness of limiting fat intake was set as a
189	counterfactual mediator. We used a linear regression model to analyze the association
190	with the mediator. ²⁷ We represented the sum of the effects of controlled direct effect and
191	reference interaction as direct effect, and the sum of the effects of mediated interaction
192	and pure indirect effect as indirect effect.
193	All statistical analyses were performed using Stata software version 17 (Stata Corp,
194	College Station, TX). The statistical significance level was set at 5%.

196 RESULTS

197 Sex differences for each variable were evaluated by χ^2 -test for categorical variables and 198 t-test for continuous variables, and the proportion of participants in the age group of 60-199 69 years was the highest for both men and women (Table 1). The prevalence of current 200 smoker, current alcohol drinker, obesity, hypertension, impaired glucose tolerance, and 201 dyslipidemia were higher in men than in women. In addition, women tended to show 202 higher prevalence in the awareness of limiting each food intake; there were statistically

203	significance in these differences between men and women, except for awareness of
204	limiting sweets intake.
205	The distributions of age, BMI, and awareness of limiting intake of fat, and sweets, were
206	statistically different between groups with and without awareness of limiting energy
207	intake (eTable 1). For the comparison between groups by the awareness of limiting fat
208	intake, the distributions of all variables were significantly different (eTable 2). Similar
209	analyses were conducted for awareness of limiting sweets intake. All variables shown in
210	the Tables were significantly related to awareness (eTable 3).
211	For both men and women, study participants with awareness of limiting energy intake
212	consumed lower FFQ-based estimated energy intake than those without this awareness;

- 213 similarly, those with awareness of limiting fat intake showed lower fat intake than those
- 214 without this awareness (Table 2). Furthermore, both men and women with awareness of
- 215 limiting sweets intake consumed less energy and fat than those without this awareness,
- 216 except for fat intake in women.

- 217 We checked the biasing paths that affect the causal path between awareness of limiting
- food intake and all-cause mortality using DAGs and included the factors related to the 218
- 219 biasing paths as covariates in the statistical model. In men, awareness of limiting energy
- 220 intake was associated with a decreased mortality risk (HR=0.79; 95% CI, 0.71 to 0.88) in

221	Model 1 (adjusted for age only); in the subclass analysis by BMI, this result was
222	significant for BMI <18.5 kg/m ² and BMI 18.5-24.9 kg/m ² . However, these associations
223	disappeared in Model 2 (adjusted for lifestyle-related confounding factors, awareness of
224	limiting intake of fat and sweets) (Table 3). In women, on the other hand, awareness of
225	limiting energy intake was associated with an increased mortality risk (HR=1.39; 95% CI,
226	1.06 to 1.81) in Model 2; in the subclass analysis, this association was stronger in those
227	with BMI $\geq 25.0 \text{ kg/m}^2$ (HR=1.93; 95% CI, 1.13 to 3.27).
228	Although awareness of limiting fat intake was negatively associated with male
229	mortality risk (HR=0.79; 95% CI, 0.72 to 0.88), this significant association disappeared
230	in Model 2 (adjusted for lifestyle-related confounding factors; awareness of limiting
231	intake of energy and sweets; and the presence of dyslipidemia or hypertension) (Table 4).
232	Similar tendencies were observed regardless of the presence of dyslipidemia, presence of
233	dyslipidemia without medication, and BMI of 18.5-24.9 kg/m ² . In women, awareness of
234	limiting fat intake was significantly associated with a decreased mortality risk even after
235	adjusting for all confounding variables (HR=0.73; 95% CI, 0.55 to 0.94) (Model 2).
236	In the mediation analysis for women, the coefficients (Coef.) for direct and total effects
237	of awareness of limiting fat intake on all-cause mortality were significant, at -0.27 (95%
238	CI, -0.47 to -0.08) and -0.27 (95% CI, -0.46 to -0.07), respectively, after adjusting the

effects of covariates used in Table 4. In contrast, the indirect effect was not statistically

240 significant (Coef.=0.008; 95% CI, -0.001 to 0.016).

241 Awareness of limiting sweets intake was significantly associated with a decreased mortality risk among men (Model 1 in Table 5). In the subclass analysis of Model 1 242 243 among men, similar negative associations were observed in those without glucose 244 intolerance and in those with glucose intolerance without medication. However, again, 245 this association disappeared after adjusting for the effects of potential confounding factors 246 (Model 2 in Table 5). Similar results were observed among women without glucose intolerance and those with a BMI of 18.5-24.9 kg/m². In men with glucose intolerance, 247 248 awareness of limiting sweet intake was marginally related to the increase of all-cause 249 mortality in Model 2 (HR=1.29; 95% CI, 0.99 to 1.69).

250

251 **DISCUSSION**

This study evaluated the association between awareness of limiting food intake and allcause mortality in the general Japanese population. Significant negative associations
between awareness of limiting fat intake and mortality were observed in the women.
Mediation analysis revealed that this association was not mediated by actual fat intake.

256 On the other hand, awareness of limiting energy intake was associated with an increased 257 mortality risk in women, and this association was stronger in those with BMI ≥ 25.0 kg/m². 258 Response to the questionnaire regarding awareness of limiting food intake was subjective in nature; as such, positive responses were not necessarily accompanied by 259 260 actual restrictions in dietary behavior. Therefore, we conducted a mediation analysis to 261 determine whether awareness of limiting fat intake led to lower mortality via actual fat 262 intake reduction. The results of the mediation analysis showed that awareness of limiting fat intake, rather than actual reduction in fat intake, was significantly associated with 263 264 lower all-cause mortality, especially among women. These results suggest that 265 individuals with higher dietary awareness may have higher overall health awareness and 266 healthier behaviors beyond dietary behaviors, and that this may be associated with lower 267 all-cause mortality. This trend was more pronounced among women. Health consciousness and related-behaviors are not always in accordance. For example, 268 269 it has been reported that the self-reported consumption of alcohol is underestimated.²⁸ 270 Furthermore, self-reported smoking rates tend to be underestimated, based on a literature review.²⁹ In contrast, the amount of exercise is reported as overestimated.³⁰ Further, self-271 reported food intake does not necessarily match the actual intake.³¹ The behavioral change 272 273 stage model has five stages; precontemplation, contemplation, preparation, action, and

maintenance; the stage with healthy awareness but without healthy behavior corresponds
to a period of contemplation or preparation this model.⁵ As detailed in the introduction,
campaigns in various countries have targeted awareness to promote healthy behavioral
changes. Although studies suggest the success of these campaigns in increasing
awareness and improving behavior, to the best of our knowledge, no study has evaluated
the association between awareness of limiting food intake and mortality risk.

281 Energy intake

282 In the present study, the estimated energy intake by FFQ was lower in those with 283 awareness of limiting energy intake than in those without this awareness. However, in 284 Model 2, women with awareness of limiting energy intake showed an increased mortality risk (HR=1.39; 95% CI, 1.06 to 1.81), especially in those with BMI ≥ 25.0 kg/m² 285 (HR=1.93; 95% CI, 1.13 to 3.27). These inconsistent results might be due to a causal 286 287 reversal phenomenon, in which participants with background risk factors for excessive 288 energy intake (e.g., high BMI) at the time of the baseline survey had energy intake restriction awareness, resulting in the observed increased mortality risk. To confirm this 289 290 possibility, we re-conducted the same analyses after excluding the participants with either 291 hypertension, dyslipidemia, or hyperglycemia at baseline surveys, and the results were

almost same, except that the estimate of HR for obese women with BMI ≥25.0 kg/m² was
much higher, at 4.37 (95% CI, 1.06 to 18.03). Detailed analysis including data by cause
of death is needed in the future.
Fat intake
Fat intake has been reported to have a linear positive or U-shaped association with

mortality.^{3,32} Regarding the association between awareness and behavior pertaining to fat
intake, a previous study reported that subjective and objective assessments of fat intake
did not match in both evaluated samples, reflecting the general population in the
Netherlands and adults in the United States.³³ In addition, it has been reported that fat
intake, as well as energy intake, is reduced by food labeling.¹³

In the present study, the estimated fat intake by the FFQ was lower in those with awareness of limiting fat intake than in those without this awareness. Although no significant association was found between awareness of limiting fat intake and all-cause mortality in men (Model 2), a significant negative association was observed among women (HR=0.73; 95% CI, 0.55 to 0.94 in Model 2). Moreover, a similar negative association was observed in women with obesity (HR=0.62; 95% CI, 0.37 to 1.05 in Model 2). The mediation analysis revealed that these associations were not significantly

310	mediated by actual fat intake, while significant negative associations were found for the
311	direct and total effects for awareness of limiting fat intake on mortality risk.
312	Although a significant bias could occur if those with awareness of limiting food intake
313	responded to the FFQ more conservatively than their actual intake, the results of the
314	mediation analysis indicate that the effect via fat intake obtained from the FFQ was not
315	significant. In other words, even if participants indicated a lower fat intake on the FFQ
316	than their actual fat intake, other mechanisms might be responsible for the decline in all-
317	cause mortality.
318	

319 Sweet food intake

- 320 In previous studies, excessive intake of added sugar³⁴ and total sugar were associated with
- 321 increased mortality risk.⁴ In contrast, another study reported no significant association
- 322 between eating patterns for sweet foods and mortality.³⁵

The current study did not find a significant association between awareness of limiting sweets intake and a decrease in all-cause mortality risk. There are two potential explanations for this result. Firstly, it may be due to the infrequency of eating sweet foods relative to the energy and fat intake in the daily diet; as a result, the intake of sweet foods may have less impact on mortality. In fact, the percentage of those who consumed cakes

328	and Japanese cake daily was quite small in the current study, comprising 0.2% of those
329	with awareness of limiting sweet foods and 0.1% of those without this awareness.
330	Secondly, we only had information on the frequency of sweet food intake, disallowing a
331	detailed quantitative assessment and mediation analysis. Since a lot of sugar is consumed
332	from foods other than cakes, such as sweets, breads, and soft drinks, future studies should
333	take this consumption into account as well.
334	Only men with glucose intolerance showed a marginally significant positive
335	association between awareness of limiting sweets intake and all-cause mortality in Model
336	2 (HR=1.29; 95% CI, 0.99 to 1.69). This trend was enhanced among the participants with
337	medication. Although a more detailed analysis is needed, these results suggest that there
338	may be residual effects of causal reversal in the relationship between awareness of
339	limiting sweet foods and all-cause mortality risk in men with impaired glucose tolerance.
340	
341	Strengths and limitations

Strengths and limitations

To the best of our knowledge, this is the first study to examine associations between 342 awareness of limiting food intake and the risk of mortality in a relatively large number of 343 participants from the general population. 344

345	However, as a limitation of the present study, although this was a prospective study,
346	the age at baseline was 35–69 years. Some participants already had a condition requiring
347	dietary restrictions at baseline, which may have contaminated the results (e.g. resulting in
348	causal reversal). Therefore, we performed subclass analyses, excluding populations with
349	underlying diseases requiring dietary restrictions. Furthermore, we adjusted for
350	confounding factors using information on a wide range of lifestyle factors and medical
351	examination results; however, the effects of host factors and unspecified confounding
352	factors are unknown. Further, the results did not change even when categories were
353	further divided. In addition, the present study targeted participants who underwent
354	medical examinations and voluntary responded to mailed fliers. Accordingly, the
355	proportion of participants with high health consciousness may be higher than that in the
356	general population, and the results may be slightly overestimated.
357	Awareness of limiting food intake might be influenced by a history of disease and
358	other factors. Subjective stress was considered a potential confounding factor, but
359	adjusting for simple subjective stress status at baseline (having experienced strong stress
360	in the past year or not) did not affect the main results. We attempted to distinguish the
361	effects of underlying health conditions from those of awareness by subclass analyses;
362	however, we could not adjust for the effects of other unknown factors. Moreover, some

363	participants may have been dieting, which is a potential confounding factor, but this
364	information was not available.
365	In this study, actual fat intake was used as the most likely mediator in the mediation
366	analysis of the awareness of limiting fat intake. However, since the study design was a
367	cross-sectional study and the temporal order of causes and mediators was not ensured, it
368	may not have been sufficiently assessed as a mediator, which is one of the limitations of
369	this study.
370	Sugar intake was not evaluated as a nutrient since only frequency information for cake
371	and Japanese cake was collected by the FFQ used in this study. Lastly, we could not
372	consider salt intake in this study because of the low validity of salt intake by FFQ.
373	
374	CONCLUSIONS
375	This study examined the association between awareness of limiting food intake and all-
376	cause mortality in the Japanese general population. Awareness of limiting fat intake was
377	associated with lower risk of all-cause mortality only in women, and this association was
378	not mediated by actual fat intake. On the other hand, awareness of limiting intake of
379	energy and sweets did not reduce the risk of all-cause mortality. These results suggest

that awareness of limiting food intake has a limited effect on all-cause mortality risk, and

this relationship may reflect not only dietary habits, but also other behavioral changes and

382 overall health awareness.

383

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- 404 and approved the final manuscript to be published.
- 405

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406 Figure legends

407 eFigure 1

White: adjusted variable; pink: ancestor of exposure and outcome; light gray: unobserved
(latent); green with a black mark inside: exposure; blue with a black mark inside:
outcome; blue: ancestor of outcome; green arrow: causal path.

411

412 eFigure 2

413 White: adjusted variable; pink: ancestor of exposure and outcome; light gray: unobserved

414 (latent); green with a black mark inside: exposure; blue with a black mark inside:

415 outcome; blue: ancestor of outcome; green arrow: causal path.

416

417 eFigure 3

418 White: adjusted variable; pink: ancestor of exposure and outcome; light gray: unobserved

419 (latent); green with a black mark inside: exposure; blue with a black mark inside:

420 outcome; blue: ancestor of outcome; green arrow: causal path.

421

422

	Μ	Men		Women			
	N=2'	7,294	N=31	N=31,478			
		N	(%)				
Age (years)							
35-49	6,383	(23.4)	8,057	(25.6)			
50-59	8,993	(33.0)	11,031	(35.0)	<0.001		
60-69	11,918	(43.7)	12,390	(39.4)			
Years of education (≥16 years)	7,644	(36.1)	2,486	(10.9)	<0.001		
Current smoker	8,201	(30.1)	2,032	(6.5)	<0.001		
Current alcohol drinker	20,897	(76.6)	11,266	(35.8)	<0.001		
Obese (BMI \geq 25.0 kg/m ²)	8,236	(30.2)	5,922	(18.8)	<0.001		
Daily activity (≥15.0 METs · h/day)	8,637	(31.7)	9,506	(30.3)	<0.001		
Habitual exercise (≥2.19 METs • h/day)	8,126	(30.7)	8,136	(27.0)	<0.001		
Hypertension	16,577	(60.7)	14,684	(46.7)	<0.001		
Glucose intolerance	8,299	(30.4)	6,617	(21.0)	<0.001		
Dyslipidemia	11,555	(42.3)	8,638	(27.4)	<0.001		
Food intake							
Beef and pork (≥3 times/week)	7,709	(28.3)	13,318	(42.4)	<0.001		
Green & yellow vegetable (≥3 times/week)	11,553	(42.4)	17,873	(56.9)	<0.001		
Fruits (≥3 times/week)	6,763	(24.8)	13,910	(44.2)	<0.001		
Cake (≥1 time/week)	4,939	(18.3)	8,506	(27.3)	<0.001		
Japanese cake (≥1 times/week)	7,447	(27.3)	15,204	(48.3)	<0.001		
Awareness of limiting food intake							
Energy	9,219	(33.8)	12,379	(39.3)	<0.001		
Fat	10,306	(37.8)	14,485	(46.0)	<0.001		
Sweets	9,176	(33.6)	10,758	(34.2)	0.155ª		
Three awareness (Yes) responses	6,567	(24.1)	8,679	(27.6)	<0.001		
One to three awareness (Yes) responses	12,775	(46.8)	16,438	(52.2)	<0.001		
	Mean (SD)						
Nutritional intake							
Energy (kcal/day)	1939.0	(356.1)	1553.7	(230.6)	<0.001		
Fat (gram/day)	42.6	(11.0)	44.8	(10.8)	<0.001		

Table 1. Characteristics of the study population according to sex

BMI, body mass index; MET, metabolic equivalent of task

 aP values obtained by χ^2 test.

^bP values obtained by t-test.

	Mean of estimated intake (95% CI)								
	Awareness of limiting energy intake			Awareness of limiting fat intake			Awareness of limiting sweets intake		
	No	Yes	Р	No	Yes	Р	No	Yes	Р
Men									
Energy intake (kcal)	1959.4	1899.0	<0.001 ^a	1955.2	1912.3	<0.001 ^a	1951.1	1915.1	<0.001ª
	(1954.1-1964.8) (1892.2-1905.8)			(1949.7-1960.7) (1905.8-1918.8)			(1945.9-1956.4) (1908.1-1922.0)		
Fat intake (gram)	42.7	42.3	0.791 ^b	42.9	42.0	<0.001 ^b	42.9	42.0	0.001 ^b
	(42.6-42.9)	(42.1-42.5)		(42.8-43.1)	(41.8-42.2)		(42.7-43.1)	(41.7-42.2)	
Women									
Energy intake (kcal)	1568.9	1530.3	<0.001 ^a	1565.7	1539.6	<0.001 ^a	1564.2	1533.5	<0.001ª
	(1565.5-1572.2)	(1526.4-1534.3)	(1562.2-1569.3)	(1536.0-1543.2)	(1561.0-1567.4)	(1529.3-1537.6)
Fat intake (gram)	44.9	44.6	0.025^{b}	45.1	44.4	<0.001 ^b	45.1	44.3	0.196 ^b
	(44.8-45.1)	(44.4-44.8)		(45.0-45.3)	(44.2-44.5)		(44.9-45.2)	(44.1-44.5)	

BMI, body mass index; CI, confidence interval

^aAdjusted for age, BMI, region, smoking habit, alcohol drinking habit, years of education, daily activity, habitual exercise.

^bAdjusted for age, BMI, region, smoking habit, alcohol drinking habit, years of education, daily activity, habitual exercise, energy intake.

	Events	Person-	Hazard ratio	o (95% CI) *
	(n)	years	Model 1	Model 2
Men				
Awareness (No)	1,243	196,503	1.00	1.00
Awareness (Yes)	444	93,725	0.79 (0.71-0.88)	0.89 (0.74-1.07)
BMI (kg/m ²)				
<18.5				
Awareness (No)	91	6,374	1.00	1.00
Awareness (Yes)	8	1,157	0.47 (0.23-0.97)	0.51 (0.16-1.66)
18.5-24.9				
Awareness (No)	808	133,360	1.00	1.00
Awareness (Yes)	281	61,249	0.79 (0.69-0.90)	0.84 (0.67-1.06)
≥25.0				
Awareness (No)	344	56,770	1.00	1.00
Awareness (Yes)	155	31,319	0.89 (0.73-1.08)	0.99 (0.72-1.38)
Women				
Awareness (No)	557	218,022	1.00	1.00
Awareness (Yes)	272	126,458	0.95 (0.82-1.10)	1.39 (1.06-1.81)
BMI (kg/m ²)				
<18.5				
Awareness (No)	42	19,802	1.00	1.00
Awareness (Yes)	11	7,716	0.77 (0.39-1.52)	0.78 (0.25-2.42)
18.5-24.9				
Awareness (No)	382	157,992	1.00	1.00
Awareness (Yes)	172	92,648	0.87 (0.72-1.04)	1.30 (0.94-1.80)
≥25.0				
Awareness (No)	133	40,228	1.00	1.00
Awareness (Yes)	89	26,095	1.16 (0.88-1.53)	1.93 (1.13-3.27)

Table 3. Association b	between awareness	of limiting energy	intake and all	-cause mortality

BMI, body mass index; CI, confidence interval; HR, hazard ratio

*Hazard ratio due to the awareness of limiting energy intake

Model 1: Adjusted for age.

Model 2: Adjusted for age; BMI; region; smoking habit; alcohol drinking habit; years of education; daily activity; habitual exercise; meat, green vegetable, and fruit intake; awareness of limiting fat and sweet food intake.

	Events	Person-	Hazard ratio (95% CI) *			
	(n)	years	-	Model 1	Ν	Model 2
Men						
Awareness (No)	1,166	184,743	1.00		1.00	
Awareness (Yes)	521	105,485	0.79	(0.72-0.88)	0.95	(0.79-1.14)
Dyslipidemia						
No						
Awareness (No)	617	107,148	1.00		1.00	
Awareness (Yes)	243	58,510	0.72	(0.62-0.84)	0.93	(0.72-1.20)
Yes						
Awareness (No)	549	77,595	1.00		1.00	
Awareness (Yes)	278	46,974	0.86	(0.74-0.99)	0.99	(0.76-1.28)
Among participants w	ith dyslip	idemia				
Medication (No)						
Awareness (No)	452	65,362	1.00		1.00	
Awareness (Yes)	182	33,187	0.83	(0.70-0.99)	1.00	(0.74-1.35)
Medication (Yes)						
Awareness (No)	97	12,234	1.00		1.00	
Awareness (Yes)	96	13,788	0.97	(0.73-1.29)	0.85	(0.48-1.48)
BMI (kg/m ²)						
<18.5						
Awareness (No)	85	5,888	1.00		1.00	
Awareness (Yes)	14	1,643	0.60	(0.34-1.06)	1.04	(0.41-2.68)
18.5-24.9						
Awareness (No)	756	124,990	1.00		1.00	
Awareness (Yes)	333	69,619	0.80	(0.70-0.91)	0.97	(0.77-1.21)
≥25.0						
Awareness (No)	325	53,866	1.00		1.00	
Awareness (Yes)	174	34,223	0.87	(0.72-1.04)	0.92	(0.66-1.28)
Women						
Awareness (No)	531	194,956	1.00		1.00	
Awareness (Yes)	298	149,524	0.80	(0.69-0.92)	0.73	(0.55-0.94)

Table 4. Association between awareness of limiting fat intake and all-cause mortality

Dyslipidemia

No

351	142,417	1.00		1.00	
189	104,805	0.79	(0.66-0.95)	0.74	(0.54-1.03)
180	52,539	1.00		1.00	
109	44,719	0.80	(0.63-1.02)	0.69	(0.42-1.12)
ith dyslip	oidemia				
102	35,359	1.00		1.00	
55	23,088	0.90	(0.64-1.25)	0.62	(0.32-1.18)
78	17,181	1.00		1.00	
54	21,631	0.69	(0.48-0.99)	0.60	(0.27-1.30)
38	17,435	1.00		1.00	
15	10,082	0.77	(0.42-1.42)	0.73	(0.27-1.96)
359	141,284	1.00		1.00	
195	109,356	0.76	(0.64-0.91)	0.76	(0.55-1.05)
134	36,237	1.00		1.00	
88	30,086	0.88	(0.67-1.15)	0.62	(0.37-1.05)
	189 180 109 ath dyslip 102 55 78 54 38 15 359 195 134	189 104,805 180 52,539 109 44,719 101 35,359 55 23,088 78 17,181 54 21,631 38 17,435 15 10,082 359 141,284 195 109,356 134 36,237	189 104,805 0.79 180 52,539 1.00 109 44,719 0.80 101 44,719 0.80 102 35,359 1.00 55 23,088 0.90 78 17,181 1.00 54 21,631 0.69 38 17,435 1.00 15 10,082 0.77 359 141,284 1.00 195 109,356 0.76 134 36,237 1.00	189104,805 0.79 $(0.66-0.95)$ 180 $52,539$ 1.00 10944,719 0.80 $(0.63-1.02)$ 101 $35,359$ 1.00 102 $35,359$ 1.00 55 $23,088$ 0.90 $(0.64-1.25)$ 78 $17,181$ 1.00 54 $21,631$ 0.69 $(0.48-0.99)$ 38 $17,435$ 1.00 15 $10,082$ 0.77 $(0.42-1.42)$ 359 $141,284$ 1.00 195 $109,356$ 0.76 $(0.64-0.91)$ 134 $36,237$ 1.00	189 $104,805$ 0.79 $(0.66-0.95)$ 0.74 180 $52,539$ 1.00 1.00 109 $44,719$ 0.80 $(0.63-1.02)$ 0.69 102 $35,359$ 1.00 1.00 55 $23,088$ 0.90 $(0.64-1.25)$ 0.62 78 $17,181$ 1.00 1.00 54 $21,631$ 0.69 $(0.48-0.99)$ 0.60 38 $17,435$ 1.00 1.00 15 $10,082$ 0.77 $(0.42-1.42)$ 0.73 359 $141,284$ 1.00 1.00 195 $109,356$ 0.76 $(0.64-0.91)$ 0.76 134 $36,237$ 1.00 1.00

BMI, body mass index; CI, confidence interval; HR, hazard ratio

*Hazard ratio due to the awareness of limiting fat intake

Model 1: Adjusted for age.

Model 2: Adjusted for age; BMI; region; smoking habit; alcohol drinking habit; years of education; daily activity; habitual exercise; meat, green vegetable, and fruit intake; awareness of limiting energy and sweet food intake; dyslipidemia and hypertension.

	Events	Person-	Hazard ratio	o (95% CI) *
	(n)	years	Model 1	Model 2
Men				
Awareness (No)	1,201	196,493	1.00	1.00
Awareness (Yes)	486	93,735	0.87 (0.78-0.97)	1.10 (0.92-1.31)
Glucose intolerance				
No				
Awareness (No)	785	144,475	1.00	1.00
Awareness (Yes)	219	55,993	0.76 (0.65-0.88)	0.96 (0.75-1.22
Yes				
Awareness (No)	416	52,018	1.00	1.00
Awareness (Yes)	267	37,742	0.93 (0.80-1.09)	1.29 (0.99-1.69
Among participants with g	glucose into	olerance		
Medication (No)				
Awareness (No)	317	45,229	1.00	1.00
Awareness (Yes)	154	27,911	0.82 (0.68-1.00)	1.12 (0.82-1.54
Medication (Yes)				
Awareness (No)	99	6,789	1.00	1.00
Awareness (Yes)	113	9,831	0.91 (0.69-1.20)	1.43 (0.81-2.52)
BMI (kg/m ²)				
<18.5				
Awareness (No)	87	6,178	1.00	1.00
Awareness (Yes)	12	1,352	0.56 (0.31-1.04)	1.15 (0.45-2.90
18.5-24.9				
Awareness (No)	777	134,007	1.00	1.00
Awareness (Yes)	312	60,602	0.90 (0.78-1.02)	1.18 (0.95-1.47
≥25.0				
Awareness (No)	337	56,307	1.00	1.00
Awareness (Yes)	162	31,782	0.90 (0.75-1.09)	0.99 (0.72-1.37
Women				
Awareness (No)	585	233,237	1.00	1.00
Awareness (Yes)	244	111,243	0.90 (0.78-1.05)	0.94 (0.73-1.21

Table 5. Association between awareness	of limiting sweets i	intake and all-cause mortality

Glucose intolerance

No

426	185,536	1.00	1.00
137	81,850	0.76 (0.63-0.93)	0.85 (0.62-1.16)
159	47,702	1.00	1.00
107	29,393	1.16 (0.90-1.49)	1.12 (0.72-1.73)
ose into	lerance		
133	44,461	1.00	1.00
77	24,560	1.10 (0.83-1.47)	1.00 (0.62-1.60)
26	3,241	1.00	1.00
30	4,833	0.93 (0.54-1.60)	1.31 (0.43-4.06)
41	20,917	1.00	1.00
12	6,600	1.00 (0.52-1.92)	1.61 (0.52-4.98)
405	170,751	1.00	1.00
149	79,889	0.80 (0.67-0.97)	0.84 (0.62-1.15)
139	41,569	1.00	1.00
83	24,754	1.08 (0.82-1.43)	1.09 (0.67-1.79)
	137 159 107 oose into 133 77 26 30 41 12 405 149 139	137 81,850 159 47,702 107 29,393 sose intolerance 133 44,461 77 24,560 26 3,241 30 4,833 41 20,917 12 6,600 405 170,751 149 79,889 139 41,569	137 $81,850$ $0.76 (0.63-0.93)$ 159 $47,702$ 1.00 107 $29,393$ $1.16 (0.90-1.49)$ ose intolerance 133 $44,461$ 133 $44,461$ 1.00 77 $24,560$ $1.10 (0.83-1.47)$ 26 $3,241$ 1.00 30 $4,833$ $0.93 (0.54-1.60)$ 41 $20,917$ 1.00 12 $6,600$ $1.00 (0.52-1.92)$ 405 $170,751$ 1.00 149 $79,889$ $0.80 (0.67-0.97)$ 139 $41,569$ 1.00

BMI, body mass index; CI, confidence interval; HR, hazard ratio

*Hazard ratio due to the awareness of limiting sweets intake

Model 1: Adjusted for age.

Model 2: Adjusted for age; BMI; region; smoking habit; alcohol drinking habit; years of education; daily activity; habitual exercise; meat, green vegetable, and fruit intake; awareness of limiting energy and fat intake; and glucose intolerance.