A genome-wide association study on meat consumption in a Japanese population: the Japan Multi-Institutional Collaborative Cohort study

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Abbreviations: ALDH2: aldehyde dehydrogenase 2; BMI: body mass index; FFQ: food frequency questionnaire; GWAS: genome-wide association study; J-MICC: Japan Multi-Institutional Collaborative Cohort; PCA: principal component analysis; Q-Q: quantile-quantile; SNP: single nucleotide polymorphism

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Recent genome-wide association studies (GWAS) on the dietary habits of the Japanese population have shown that an effect rs671 allele was inversely associated with fish consumption, whereas it was directly associated with coffee consumption. Although meat is a major source of protein and fat in the diet, whether genetic factors that influence meat-eating habits in healthy populations are unknown. This study aimed to conduct a GWAS to replicate the results of the GWAS on meat consumption in samples of European ancestry in a Japanese population.

**Abstract**

Genome-wide association study: Meat consumption: Rs671

**Methods**

Study population

This cross-sectional study was conducted with participants aged from 35 to 69 years as part of the Japan Multi-Institutional Collaborative Cohort (J-MICC) study that started in 2005 to investigate gene-environment interactions in lifestyle-related diseases. We used the data ver. 20180112. The 14,539 participants in the J-MICC study were recruited from twelve different areas throughout Japan between 2004 and 2014. Details of the J-MICC study were reported elsewhere. Briefly, participants completed a questionnaire about lifestyle and medical information and gave a blood sample at the time of the baseline survey. The J-MICC study participants included community citizens, first-visit patients to a cancer hospital and health check examinees. All participants in this study gave written informed consent, and the study protocol was approved by the Research Ethics Committees of Aichi Cancer Center, Nagoya University Graduate School of Medicine, and the other institutions participating in the J-MICC study. The present study was conducted according to the principles expressed in the World Medical Association Declaration of Helsinki.

Of 14,539 participants, 448 were excluded based on the GWAS screening described in the ‘Genotyping and quality control filtering’ section. Of the remaining 14,091 participants, two withdrew from the study afterwards, three were outside of the study age range, seven had daily energy intake less than 500 kcal or greater than 5000 kcal and three with missing nutritional data were excluded. As a result, we analysed the data of 14,076 participants in the present study.

**Questionnaire and measurements**

The questionnaire for the J-MICC studies included questions about medical history, height, weight, smoking and drinking habits, and dietary habits. The questionnaire was checked by...
experienced staff to confirm completeness and consistency. Height and weight measurements and blood sampling were conducted as part of a health check-up or for research purposes at the institutions participating in the J-MICC study (39). Question items were collected using a scientifically validated self-administered questionnaire (20–25). Body mass index (BMI) was calculated by dividing body weight in kilograms by the square of height in metres.

**Dietary assessment**

We used a semi-quantitative food frequency questionnaire (FFQ) to estimate food intake that has been reported previously (20–25). We chose twenty foods/food groups and beverages (shown as <number>) including <1> rice, <2> bread, <3> noodles, <4> potatoes, <5> soybeans, <6> soybean-paste, <7> green-yellow vegetables, <8> other vegetables, <9> fruit, <10> mushrooms, <11> seaweed, <12> fish and other seafood, <13> meat (chicken, beef or pork, liver, ham group [including sausage, salami and bacon]), <14> eggs, <15> milk, <16> oils, <17> confectionery, <18> green tea, <19> coffee and <20> alcoholic beverages. Food intake frequencies were classified into eight categories (never or seldom, one to three times per month, one to two times per week, three to four times per week, five to six times per week, once a day, twice a day and three or more times a day, which were converted into 0, 0.5, 1, 2, 3 before analysis). For each food category, the frequency was multiplied by the portion size, and the total intake amount was calculated. For the present study, total meat consumption was extracted. Energy intake by FFQs was estimated by using the Standard Tables of Food Composition in Japan, 5th edition (36). Total alcohol intake was estimated as the sum of pure alcohol intake. The frequency of alcohol intake was obtained in six categories (never or seldom, one to three times per month, one to two times per week, three to four times per week, five to six times per week and every day). Total alcohol consumption (g/d) was estimated as the summed amount of pure alcohol consumption.

**Genotyping and quality control filtering**

Buffy coat fractions and DNA were prepared from blood samples and stored at −80 °C at the central J-MICC Study office. DNA was extracted from all buffy coat fractions using a BioRobot M48 Workstation (Qiagen Group, Tokyo, Japan) at the central study office. For the samples from two areas (Fukuoka and Kyushu and the Okinawa Population Study [KOPS]), DNA was extracted locally from samples of whole blood using an automatic nucleic acid isolation system (NA-3000, Kurabo, Co., Ltd, Osaka, Japan). The 14 539 study participants from the thirteen areas of the J-MICC study were genotyped at the RIKEN Center for Integrative Medicine Sciences using a HumanOmnExpressExome-8v1.2 BeadChip array (Illumina Inc., San Diego, CA, USA). Twenty-six participants with inconsistent sex information between the questionnaire and the estimate from genotyping were excluded. The identity-by-descent method in the PLINK 1.9 software (27,28) identified 388 close relationship pairs (pi-hat > 0.1875), and one sample from each pair of the 388 was excluded. PCA (29) with a 1 000 Genomes reference panel (phase 3) (30) detected thirty-four participants whose estimated ancestries were outside the Japanese population (31). These thirty-four participants were excluded. In the remaining 14 091 participants, SNPs with a genotype call rate of <0.98 and/or a Hardy–Weinberg equilibrium exact test \( P < 1 \times 10^{-6} \), a low minor allele frequency (MAF) <0.01 or a departure from the allele frequency computed from the 1 000 Genomes Phase 3 EAS samples were excluded. The quality control filtering resulted in 14 091 individuals and 574 423 SNPs.

**Genotype imputation**

Genotype imputation was performed using SHAPEIT (32) and Minimac3 softwares (33) based on the 1 000 Genomes Phase 3 all ancestries as a reference panel (30). After genotype imputation, strict quality control filters were applied; namely, variants with an \( R^2 < 0.3 \) were excluded, resulting in 12 617 547 variants. Finally, 4 112 564 variants with MAF <0.01 in patients were removed, resulting in 8 503 383 variants for the analysis. We used the DosageConvertor software (34) to convert dosage files in VCF formats from Minimac3 to PLINK formats.

**Power calculations to test for an association between total meat intake and SNPs**

Statistical power to detect a true association was calculated by the method of Delongchamp et al. (38), based on the number of participants and genetic data of the discovery phase J-MICC study. The required non-centrality parameter was obtained by the equation A4 listed in Appendix A by Visscher et al. (36). When then the number of participants is 14 076, with fourteen covariates for adjustment, 0.8 for linkage disequilibrium (LD) \( R^2 \), 0.2 for MAF, 0.02 for a squared standardised \( \beta \) estimate and 8 500 000 for variants analysed, the statistical power is calculated as 0.992 according to the method proposed by Delongchamp et al. (38).

**Association analyses between genetic variants and total meat intake**

Associations between all imputed variants and total meat intake were analysed by linear regression assuming the additive effects of the allele dosage on total meat intake per 1 000 kcal energy intake (g/1 000 kcal per d) adjusted for age, sex, and PCA components 1–10 using the PLINK 1.9 software (27,28). We also performed a sex-stratified linear regression analysis, because there were significant differences in dietary intake between men and women. Furthermore, we performed logistic analysis by dichotomising meat intake per 1 000 kcal at the sex-specific median in low \( v. \) high adjusted for age, sex and PCA components 1–10, because our use of semi-quantitative FFQ might not be suited to use dietary intake as an absolute continuous variable. We also performed a sex-stratified logistic analysis. Variants achieving genome-wide significance \( (P < 5 \times 10^{-8}) \) were considered as total meat intake-associated.
variants. An R package for creating a quantile-quantile (Q–Q) plot, GWAS tools, was used. For scatter plots of P-values derived from genome-wide scan results for total meat intake, the qqman software was used.

For a sensitivity analysis, associations between all imputed variants and beef and pork intake, rather than total meat intake, were analysed adjusted for the same variables as above.

In addition, replication analysis on meat intake per 1000 kcal adjusted for age, sex and PCA components 1–10 using the J-MICC samples for twenty-nine SNPs that were previously reported to be associated with total meat intake was performed.

Student’s t-tests were used to compare means between men and women.

Results

Baseline characteristics

Baseline characteristics of the total, male and female, participants are shown in Table 1. The mean age of the participants was 54.8 years, and the percentage of women was 55.0%. The mean total meat intake was 37.9 g/d. The mean total energy intake (including that from alcohol) was 1768 kcal/d, and the mean total meat intake per 1000 kcal energy intake was 22.0 g/1000 kcal per d. The means for protein, fat, carbohydrate (% of total energy) and alcohol intake (g/d) were 13.7, 25.7, 60.6% and 9.4 g/d, respectively. The mean BMI was 23.1 kg/m². The mean age, total energy intake, percentage of carbohydrate intake, alcohol intake and BMI were significantly larger in men than in women. The mean total meat intake, mean total meat intake per 1000 kcal, percentage of protein and percentage of fat intake were significantly smaller in men than in women. The median total meat intake per 1000 kcal for men and women were 15.36 and 22.65 g/1000 kcal per d, respectively.

Association analyses between total meat intake and genetic variants

In genome-wide analyses among the 8 503 383 variants adjusted for age, sex and PCA components 1–10, no variant was associated with total meat intake per 1000 kcal energy with genome-wide significance (the Q–Q plot of the observed P-values is shown in Fig. 1). The inflation factor of the genome-wide scan was 1.01 (95% CI 1.0010, 1.0131), indicating that the population structure was well adjusted. Fig. 2 shows a Manhattan plot of the results from the GWAS of meat intake (g/1000 kcal per d), which found none with genome-wide significance (P < 5 × 10⁻⁸).

A sensitivity analysis with outcome variables restricted to beef and pork consumption yielded similar results.

In a sex-stratified genome-wide linear regression analysis in men adjusted for age and PCA components 1–10, no variant was associated with total meat intake per 1000 kcal energy with genome-wide significance (the Q–Q plot of the observed P-values is shown in Supplementary Fig. S1 of Supplementary material, and a Manhattan plot of the results from the sex-stratified analysis in men is shown in Supplementary Fig. S2 of Supplementary material). However, in a sex-stratified genome-wide linear regression analysis in women, one variant, rs7166776 in 15q26.1, was marginally significantly associated with total meat intake per 1000 kcal energy (P = 5.54 × 10⁻⁸, Table 2). The Q–Q plot of the observed P-values is shown in Fig. 3, and a Manhattan plot in women is shown in Fig. 4.

In men and women combined logistic analysis by dichotomising meat intake per 1000 kcal at the sex-specific median adjusted for age, sex and PCA components 1–10, no variant was associated with low intake with genome-wide significance (the Q–Q plot of the observed P-values is shown in Supplementary Fig. S3 of Supplementary material, and a Manhattan plot is shown in Supplementary Fig. S4 of Supplementary material). Sex-stratified logistic analysis in men and women did not show any variant that was associated with low intake with genome-wide significance (a Manhattan plot in men is shown in Supplementary Fig. S5 of Supplementary material, and that in women is shown in Supplementary Fig. S6 of Supplementary material).

Replication of previously reported SNPs

The results of a replication study in our J-MICC GWAS data with adjustment for age, sex, and PCA components 1–10 on the twenty-nine SNPs that were previously reported to be associated with diet component 1, obtained by a PCA, which represented a meat-related diet, are shown in Table 3. None of the SNPs reported were statistically significant (P < 0.05/29 = 0.0017) in Bonferroni correction.

Discussion

In our previous GWAS on food consumption using the same dataset and a similar method, we found that an effect rs671 allele was inversely associated with fish consumption, whereas it was directly associated with coffee consumption. We also found one SNP in the 14q11.2 locus that was significantly associated with the Japanese food score. However, in this study based on 14 076 Japanese, we found no significant association between tested variants and total meat per 1000 kcal.
Fig. 1. A Q–Q plot (black) for the GWAS of meat intake (g/1000 kcal per d). The x-axis shows the expected $-\log_{10} P$-values under the null hypothesis. The y-axis expresses the observed $-\log_{10} P$-values obtained by a linear regression model using PLINK\(^{27,28}\). The line represents $y = x$, which corresponds to the null hypothesis. The grey shaded area expresses the 95% CI of the null hypothesis. The inflation factor ($\lambda$) is the median of the observed test statistics divided by the median of the expected test statistics ($\lambda = 1.0117$ [95% CI 1.0010–1.0131]). An R package for creating the Q–Q plot, GWAS tools, was used\(^{37}\). Chromosomal position (GRCh37/hg19).

Fig. 2. A Manhattan plot of the results from the GWAS of meat intake (g/1000 kcal per d). The x-axis indicates chromosomal positions, and the y-axis represents $-\log_{10} P$-values obtained by linear model association analysis. The software qqman was used\(^{38}\). Chromosomal position (GRCh37/hg19).
kcal energy intake, or beef and pork consumption, in a Japanese population. In a sex-stratified genome-wide linear regression analysis in women, one variant, rs7166776 in 15q26.1, was marginally significantly associated with total meat intake per 1000 kcal energy ($P = 5.54 \times 10^{-8}$). The rs7166776 SNP is an intron variant of gene LOC105370982, which is classified as a non-coding RNA, and no disorders were found for LOC105370982 gene. The sex-stratified logistic analysis in women in the present study could not replicate the association between rs7166776 and meat consumption. Thus, the finding in the stratified linear regression analysis in women is considered as a chance finding. Additionally, twenty-nine SNPs that previously reported in the different ethnicity was not replicated in the present study. Thus, these missing significant variants in the association tests may suggest the relatively small effect of the genetic factor for meat consumption in Japanese populations.

We have recently seen an increasing number of results on the dietary habits of the Japanese population. Most of the variants found were the SNP rs671, which encodes $ALDH2$, or other variants that have a high LD with rs671. For instance, an effect rs671 allele was inversely associated with fish consumption\(^{14}\), whereas it was directly associated with coffee consumption\(^{16}\). Furthermore, Matoba et al. in the BioBank Japan Project (BBJ) showed that an effect allele had a neutral association with natto and tofu consumption, and it was directly associated with green tea, milk and yogurt consumption. They also showed that an effect allele had a neutral association with vegetable and meat consumption\(^{17}\). Since BBJ is a hospital-based cohort that includes individuals affected with some of the target diseases, possible differences in dietary habits between pre-diagnosed and diseased individuals could have affected the results. Our present results from previous studies on coffee and fish consumption and the present results on meat consumption confirmed that the findings of the study by Matoba et al.\(^{17}\) in a hospital-based cohort held in a healthy population.

The reason rs671 has pleiotropic effects on food and beverage consumption in Japanese participants is not clear. Those who

### Table 2. Result of a sex-stratified genome-wide linear regression analysis in women on total meat intake per 1000 kcal

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr:BP</th>
<th>Genes</th>
<th>EA</th>
<th>NEA</th>
<th>EAFR</th>
<th>$\beta$</th>
<th>SE</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs7166776</td>
<td>15:93865045</td>
<td>LINC02207</td>
<td>C</td>
<td>G</td>
<td>0.508</td>
<td>-1.291</td>
<td>0.237</td>
<td>$5.54 \times 10^{-8}$</td>
</tr>
</tbody>
</table>

SNP, single nucleotide polymorphism; Chr, chromosome, chromosomal position (GRCh37/hg19); BP, base pair positions; EA, effect allele; NEA, non-effect allele; EAFR, effect allele frequency; $\beta$, effect size; SE, standard error of effect size.

Genome-wide analyses among the $8 \, 503 \, 383$ variants adjusted for age, sex and PCA components 1–10, one variant, rs7166776 in 15q26.1, was marginally significantly associated with total meat intake per 1000 kcal energy.

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**Fig. 3.** A Q–Q plot (black) for the sex-stratified GWAS of meat intake (g/1000 kcal per d) in women. The x-axis shows the expected $-\log_{10} P$ values under the null hypothesis. The y-axis expresses the observed $-\log_{10} P$ values obtained by a linear regression model using PLINK\(^{27,28}\). The line represents $y = x$, which corresponds to the null hypothesis. The grey shaded area expresses the 95 % CI of the null hypothesis. The inflation factor ($\lambda$) is the median of the observed test statistics divided by the median of the expected test statistics. An R package for creating the Q–Q plot, GWAS tools, was used\(^{27}\). Chromosomal position (GRCh37/hg19).
We carried out a replication study on the twenty-nine identified SNPs associated with meat intake of European participants in the study by Niarchou et al. (18).

**Table 3.** Replication analysis using the J-MICC samples for SNPs that were associated with meat intake in a previous study

<table>
<thead>
<tr>
<th>SNP</th>
<th>Chr:BP</th>
<th>Genes</th>
<th>EA</th>
<th>NEA</th>
<th>EAFR</th>
<th>β</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs3101341</td>
<td>1:72747844</td>
<td>NEGR1</td>
<td>T</td>
<td>C</td>
<td>0.800</td>
<td>−0.068</td>
<td>0.183</td>
<td>0.709</td>
</tr>
<tr>
<td>rs66495454</td>
<td>1:72748567</td>
<td>NEGR1</td>
<td>GTCCT</td>
<td>G</td>
<td>0.234</td>
<td>0.240</td>
<td>0.177</td>
<td>0.174</td>
</tr>
<tr>
<td>rs506589</td>
<td>1:177894287</td>
<td>SEC16B</td>
<td>C</td>
<td>T</td>
<td>0.270</td>
<td>0.030</td>
<td>0.165</td>
<td>0.856</td>
</tr>
<tr>
<td>rs36016753</td>
<td>1:187269477</td>
<td>-</td>
<td>A</td>
<td>G</td>
<td>0.185</td>
<td>0.243</td>
<td>0.189</td>
<td>0.198</td>
</tr>
<tr>
<td>rs10900457</td>
<td>1:205146726</td>
<td>CNTN2, RBBP5, etc.</td>
<td>A</td>
<td>G</td>
<td>0.461</td>
<td>0.144</td>
<td>0.148</td>
<td>0.330</td>
</tr>
<tr>
<td>rs62106258</td>
<td>2:417167</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>rs5786550</td>
<td>3:62560523</td>
<td>CADPS</td>
<td>T</td>
<td>C</td>
<td>0.680</td>
<td>0.085</td>
<td>0.156</td>
<td>0.586</td>
</tr>
<tr>
<td>rs7644687</td>
<td>3:89040601</td>
<td>EOGT, TMF1, etc.</td>
<td>T</td>
<td>C</td>
<td>0.064</td>
<td>0.386</td>
<td>0.299</td>
<td>0.196</td>
</tr>
<tr>
<td>rs13340130</td>
<td>3:81790970</td>
<td>GBE1</td>
<td>A</td>
<td>T</td>
<td>0.528</td>
<td>−0.002</td>
<td>0.146</td>
<td>0.990</td>
</tr>
<tr>
<td>rs701760</td>
<td>4:113439212</td>
<td>NEUROG2, LARP7</td>
<td>C</td>
<td>G</td>
<td>0.320</td>
<td>−0.371</td>
<td>0.157</td>
<td>0.018</td>
</tr>
<tr>
<td>rs300046</td>
<td>5:37081705</td>
<td>NIPBL, C5orf42, etc.</td>
<td>G</td>
<td>A</td>
<td>0.500</td>
<td>−0.163</td>
<td>0.152</td>
<td>0.282</td>
</tr>
<tr>
<td>rs10964431</td>
<td>5:92950673</td>
<td>FAM12A</td>
<td>C</td>
<td>T</td>
<td>0.614</td>
<td>−0.273</td>
<td>0.150</td>
<td>0.068</td>
</tr>
<tr>
<td>rs9379831</td>
<td>6:26175852</td>
<td>HIST1H2AC, HIST1H1E, etc.</td>
<td>A</td>
<td>C</td>
<td>0.165</td>
<td>−0.051</td>
<td>0.235</td>
<td>0.829</td>
</tr>
<tr>
<td>rs806794</td>
<td>6:26206777</td>
<td>HIST1H2AC, HIST1H1E, etc.</td>
<td>G</td>
<td>A</td>
<td>0.839</td>
<td>−0.078</td>
<td>0.238</td>
<td>0.744</td>
</tr>
<tr>
<td>rs35797675</td>
<td>7:72878044</td>
<td>FZD9, BA21B, etc.</td>
<td>G</td>
<td>T</td>
<td>0.108</td>
<td>−0.490</td>
<td>0.240</td>
<td>0.041</td>
</tr>
<tr>
<td>rs4034907</td>
<td>7:13505059</td>
<td>CNOT4, NUP205</td>
<td>G</td>
<td>A</td>
<td>0.759</td>
<td>0.128</td>
<td>0.173</td>
<td>0.459</td>
</tr>
<tr>
<td>rs10125463</td>
<td>9:15677925</td>
<td>CCDC17I</td>
<td>A</td>
<td>T</td>
<td>0.223</td>
<td>0.074</td>
<td>0.175</td>
<td>0.674</td>
</tr>
<tr>
<td>rs6478868</td>
<td>9:131927092</td>
<td>FAM73B, DOLPP1, etc.</td>
<td>C</td>
<td>T</td>
<td>0.106</td>
<td>−0.034</td>
<td>0.237</td>
<td>0.885</td>
</tr>
<tr>
<td>rs1912286</td>
<td>10:87318888</td>
<td>-</td>
<td>A</td>
<td>G</td>
<td>0.493</td>
<td>0.074</td>
<td>0.147</td>
<td>0.614</td>
</tr>
<tr>
<td>rs3909727</td>
<td>11:126587382</td>
<td>KIRREL3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>rs4759074</td>
<td>12:54664097</td>
<td>CBX5, HNRNPA1, etc.</td>
<td>T</td>
<td>C</td>
<td>0.632</td>
<td>0.312</td>
<td>0.150</td>
<td>0.038</td>
</tr>
<tr>
<td>rs12103229</td>
<td>16:74167594</td>
<td>-</td>
<td>A</td>
<td>C</td>
<td>0.360</td>
<td>−0.117</td>
<td>0.152</td>
<td>0.443</td>
</tr>
<tr>
<td>rs12232804</td>
<td>19:42677807</td>
<td>ATP1A3, GRIKS, etc.</td>
<td>T</td>
<td>C</td>
<td>0.054</td>
<td>0.599</td>
<td>0.326</td>
<td>0.066</td>
</tr>
<tr>
<td>rs4293558</td>
<td>19:45411941</td>
<td>PVRL2, TOMM440, etc.</td>
<td>C</td>
<td>T</td>
<td>0.101</td>
<td>0.392</td>
<td>0.244</td>
<td>0.109</td>
</tr>
<tr>
<td>rs388144</td>
<td>19:49250239</td>
<td>FUT2, MAMSTR, etc.</td>
<td>T</td>
<td>C</td>
<td>0.980</td>
<td>−0.097</td>
<td>0.642</td>
<td>0.880</td>
</tr>
<tr>
<td>rs79564737</td>
<td>20:43408372</td>
<td>RIMS5</td>
<td>A</td>
<td>G</td>
<td>0.535</td>
<td>−0.100</td>
<td>0.146</td>
<td>0.494</td>
</tr>
<tr>
<td>rs136528</td>
<td>22:22745262</td>
<td>-</td>
<td>C</td>
<td>G</td>
<td>0.634</td>
<td>0.105</td>
<td>0.152</td>
<td>0.491</td>
</tr>
<tr>
<td>rs139911</td>
<td>22:40704052</td>
<td>TNRC6B</td>
<td>T</td>
<td>C</td>
<td>0.461</td>
<td>−0.249</td>
<td>0.146</td>
<td>0.087</td>
</tr>
<tr>
<td>rs202637</td>
<td>22:41853928</td>
<td>ZC3H7B, TEF, etc.</td>
<td>G</td>
<td>A</td>
<td>0.954</td>
<td>0.312</td>
<td>0.349</td>
<td>0.371</td>
</tr>
</tbody>
</table>

SNP, single nucleotide polymorphism; Chr, chromosome, chromosomal position (GRCh37/hg19); EA, effect allele; NEA, non-effect allele; EAF, effect allele frequency; β, effect size; SE, standard error of effect size. NA, not available in the J-MICC data – indicates no genes hit on that SNP.

Fig. 4. A Manhattan plot of the results from the GWAS of meat intake (g/1000 kcal per d) in women. The x-axis indicates chromosomal positions, and the y-axis represents −log10 P-values obtained by linear model association analysis. The software qqman was used (179). Chromosomal position (GRCh37/hg19).
cannot tolerate alcoholic beverages may drink coffee, green tea
and milk instead. Acetaldehyde is contained in fish and gives
many foods a pleasant aroma\(^8\). Natto contains trace concentra-
tions of acetaldehyde and some detectable concentrations of etha-
ol\(^9\). Acetaldehyde in fish and ethanol in natto may produce
some unpleasant taste or smell in those with a defective
\(ALDH2\) genotype, and thus they eat smaller amounts of fish
and natto. One reason we did not find any effect of rs671 on
meat consumption may be meat may not contain any substance
that causes unpleasant taste or smell in those with a defective
\(ALDH2\) genotype. Another aspect that may be related to why
we did not find any genetic variant associated with meat con-
sumption in a Japanese population is that the development of
interaction with some foods needs some extensive dur-
ation of exposure of some foods. With the arrival of Buddhism
in the 6th century, Japanese people stopped eating meat until
the late 19th century Meiji Era. But even today, the amount of
meat consumption is far less than that in Western countries\(^7\).
This lack of exposure to meat-eating for a long duration might
have failed in the development of gene–meat-eating interaction.

This study has several limitations. We did not perform a
replication study in a different Japanese population, because
the present results were negative from a GWAS point of
view. A replication study in a European population, however,
would probably yield quite different results from those we
found in the present study, since \(ALDH2\) polymorphism is
restricted in Eastern Asian populations. Second, although we
used a semi-quantitative FFQ to estimate food intake as
reported previously\(^{10–24}\), the number of meat foods included
in the FFQ was small. Furthermore, the use of semi-
quantitative FFQ is not best suited to use dietary intake as
an absolute continuous variable, because semi-quantitative
FFQ, in general, does not reflect portion sizes accurately and
relies solely on self-report. To compensate for shortcomings,
we performed a logistic analysis by dichotomising meat
intake in low \(v\) high at sex-specific medians.

In conclusion, we found that no genetic variants, including
rs671, were associated with total meat or beef and pork con-
sumption; therefore, meat consumption was not influenced by
genetic factors in a Japanese population.

Supplementary material
The supplementary material for this article can be found at
https://doi.org/10.1017/jns.2021.49.

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