Validity of a Self-administered Food Frequency Questionnaire for the Estimation of Acrylamide Intake in the Japanese Population: The JPHC FFQ Validation Study

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ABSTRACT

Background: Acrylamide, a probable carcinogen to humans, forms during high temperature cooking. Dietary exposure to acrylamide among the Japanese population is unknown. We aimed to establish and validate a method to assess acrylamide exposure among the Japanese population using a food frequency questionnaire (FFQ) from the Japan Public Health Center-based prospective study.

Methods: Validation studies for the FFQ were conducted in 1994 (Cohort I, \( n = 215 \)) and 1996 (Cohort II, \( n = 350 \)). The 28-day dietary records (DRs) were collected over 1 year. The FFQ was distributed before and after DR collection. Data for acrylamide exposure were based on reported measurements in Japan, and calculations considered the cooking process for specific vegetables in a home setting. Spearman’s rank correlation and weighted kappa coefficients were calculated from energy-adjusted data.

Results: Mean acrylamide intake levels estimated from DRs for Cohorts I and II were 6.78 (standard deviation [SD], 3.89) \( \mu g/\text{day} \) and 7.25 (SD, 3.33) \( \mu g/\text{day} \), and corresponding levels estimated from the FFQ were 7.03 (SD, 4.30) \( \mu g/\text{day} \) and 7.14 (SD, 3.38) \( \mu g/\text{day} \), respectively. Deattenuated correlation coefficients for men and women were 0.54 and 0.48 in Cohort I and 0.40 and 0.37 in Cohort II, respectively. Weighted kappa coefficients were over 0.80 in all cases. The main contributing food groups from DRs were beverages, confectioneries, vegetables, potatoes and starches, and cereals.

Conclusions: High kappa values validate the use of FFQ in epidemiological studies. The marked contribution of cooked vegetables indicates the importance of considering household cooking methods in assessing acrylamide intake levels in the Japanese population.

Key words: acrylamide; validity; food frequency questionnaire; dietary record; cooking method

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INTRODUCTION

Acrylamide is used in the production of industrial products, such as adhesives, and is known to be contained in tobacco smoke.¹ The International Agency for Research on Cancer classified acrylamide as a probable carcinogen in humans (Group 2A) in 1994.² Subsequently, acrylamide was found in highly heated foods, such as french fries, for the first time by Swedish scientists in 2002.³ Therefore, diet is also a considerable source of acrylamide exposure in the general population.

To clarify the risk of dietary acrylamide intake on carcinogenicity in humans, epidemiological studies mainly use food frequency questionnaires (FFQs) to assess acrylamide intake. Since FFQs can be used to rank participants according to levels of intake, associations, such as those between food intake and risk of disease, can be examined. However, there has been no study establishing an acrylamide database and validating acrylamide intake estimates from FFQs in the Japanese population.

Foods contributing to acrylamide intake are expected to differ between Asian and western populations. The main foods contributing to acrylamide intake among western people are potato-based foods, wheat-based products, and coffee.⁴–⁶ However, in a report of acrylamide content in foods commonly consumed by Japanese people, foods associated with household cooking, such as stir-fried vegetables, also contained acrylamide.⁷ Therefore, the cooking method of foods prepared at home is an important consideration in the estimation of dietary acrylamide intake levels.

We oversee the Japan Public Health Center-based (JPHC) Study, a prospective study of a large Japanese cohort that was launched in the 1990s and continues to be followed today. The
present study aimed to establish a database of acrylamide-
containing foods commonly consumed by Japanese people and
to validate acrylamide intake from a self-administered dietary
questionnaire compared to a 28-day weighted dietary record (DR)
in the JPHC Study.

METHODS

Data collection and study participants
Details of the study design and participants’ characteristics were
described elsewhere. In brief, validation studies for FFQ were
conducted among subsamples from two cohorts: Cohort I from
February 1994 and Cohort II from May 1996. In the Cohort I
area, 215 participants completed 28-day (14-day for participants
in Okinawa) DRs and the FFQ, and 209 participants completed
DRs and two FFQs. In the Cohort II area, 350 participants
completed DRs and the FFQ, and 209 participants completed
DRs and two FFQs. Cohort I and Cohort II were independently
conducted studies that collected dietary records among different
populations. This study did not undergo ethics approval, since it
was conducted before the administration of ethics guidelines for
epidemiological research in Japan, which mandate such approval.
However, oral or written informed consent was obtained from
the participants before the start of the study. Further, for
statistical analysis, our study protocol was approved by the
ethics committee of Osaka University (approved number 15131).

Development of a database of acrylamide-containing foods
A total of 10 reports were available through July 2016, and
we selected the measurements in these reports according to the
following criteria: 1) sample size of measurements was two or
more; 2) mean or median value of measurements was reported or
able to be calculated from reported data; 3) if there were several
reports for the same food, values measured in a Japanese sample
and from larger sample sizes were preferentially used; 4) if both
mean and median were reported, median was preferentially used;
and 5) if the measurements were below quantitative or qualitative
limits, values equating to half that of the quantitative or
qualitative concentrations were used.

To calculate acrylamide intake from DRs, we used the
Standard Tables of Food Composition in Japan, Fifth Revised
and Enlarged Edition (5th FCT), which contains 1,878 food
items. Since acrylamide measurement values in existing literature
are limited, we attempted to organize relevant acrylamide-
containing items of the 5th FCT into more discrete categories
for which acrylamide measurements are available. We catego-
rized the 1,878 food items from the 5th FCT using the following
criteria: a) same or similar species, same or similar parts, and
same or similar cooking methods as an acrylamide-containing
food with available data; b) when a food consisted of several
foods containing acrylamide (eg, confectioneries), the acrylamide
values were calculated using measurements from the database for
each food item; further, c) oils and fats, fresh food, non-processed
food, and non-heated food were assigned a value of zero; and d)
other foods that did not meet the above criteria were treated as
missing values. After applying these acrylamide criteria to the 5th
FCT, 282 (15%) out of 1,878 food items from the 5th FCT were
designated as acrylamide-containing foods. The number of foods
treated as non-acrylamide-containing foods (criteria c) was 1,276,
and the number of foods treated as missing (criteria d) was 320.

We did not apply available acrylamide concentration data for
mixed dishes, which were not listed in the 5th FCT (eg, stir-fried
vegetables and meats, fried fish with batter, and curry), because
cooked foods listed in the 5th FCT were limited and both DR
and FFQ were conducted using food-based methods. However,
acrylamide concentration varies depending on the cooking
method, even for the same food. Therefore, in addition to the
food items from the 5th FCT, the following foods were also used
to calculate acrylamide intake from cooked foods: potatoes
depth-fried, baked, stir-fried, and stir-fried lightly as preparation),
onions (depth-fried, baked, stir-fried, and stir-fried lightly as
preparation), bean sprouts (deep-fried, baked, and stir-fried),
asparagus (deep-fried, baked, and stir-fried), sweet peppers
depth-fried, baked, and stir-fried), squash (depth-fried, baked,
and stir-fried), cabbage (deep-fried, baked, and stir-fried), string
beans (depth-fried, baked, and stir-fried), eggplant (depth-fried,
baked, and stir-fried), broccoli (depth-fried, baked, and stir-fried),
podded peas (deep-fried, baked, and stir-fried), sweet potato
depth-fried), toasted bread, deep-fried batter, and stir-fried rice.
Ultimately, we expanded the food items listed in the 5th FCT
from 1,878 to 1,917, and 321 food items (17%) were designated
as acrylamide-containing foods.

Calculation of dietary acrylamide intake from DRs
Participants recorded menus, food and beverage names, and the
amount consumed (weighed using a scale) in the specific food
diary. Dieticians checked the records and coded each food using
the food item code of the 5th FCT. To calculate acrylamide intake
from specific cooked foods not listed in the 5th FCT, dieticians
used the menu to determine the cooking methods of these foods.
Nine cooking methods (raw, boiled, deep-fried, deep-fried with
batter, baked, stir-fried, steamed, stir-fried lightly as preparation,
and unclear) were coded. Dietary acrylamide was calculated by
multiplying the concentration and amount consumed for each
food and summing these values by day. Energy intake was also
calculated using the 5th FCT.

Calculation of dietary acrylamide intake from FFQs
Our FFQ was designed to assess habitual dietary intake for the
previous 1 year. Out of 147 food items, the following 28
(19%) were designated as acrylamide-containing foods: rice,
miso, beer, baked fish paste, bread, rice cake, Japanese-style
confectioneries, cakes, biscuits and cookies, chocolates, peanuts,
fried tofu, sencha (a type of green tea), bancha (a type of green
tea), oolong tea, black tea, coffee, canned coffee, soup, potatoes,
sweet potato, onions, bean sprouts, sweet peppers, squash,
cabbage, snap beans, and broccoli. For rice, bread, potato, sweet
potato, and vegetables (onions, bean sprouts, sweet peppers, squash,
cabbage, snap beans, and broccoli), we calculated acrylamide intake by considering the cooking methods used
because our original FFQ only estimated the amount of raw food
intake. Weighted average values of acrylamide content for these
foods were calculated using the proportion of each cooking
method, obtained from the DRs of Cohort I and Cohort II
separately. We inserted the proportions of cooking method
calculated from Cohort I in the calculation of acrylamide intake in
Cohort II and vice versa. Acrylamide intake from each food was
calculated by multiplying the concentration of acrylamide for
each food by the eating frequency and portion size.

We also estimated acrylamide intake from fried batter. Our
original FFQ contained a question inquiring about eating
frequency for fried foods with batter: “How often do you consume deep fried foods with batter?” Respondents chose their response from six frequency categories: almost never, 1–3 times/month, 1–2 times/week, 3–4 times/week, 5–6 times/week, and daily. Acrylamide intake from fried batter was calculated by multiplying the eating frequency for fried foods with batter with the amount of acrylamide intake from fried batter per day calculated from the DRs. Total daily acrylamide intake from the FFQ was calculated by summing the acrylamide intake for each food item and fried batter.

### Statistical analysis
Mean dietary acrylamide intake was calculated by sex and cohort. Percentage differences of acrylamide intake between DR and FFQ were calculated using the following formula: (acrylamide intake from FFQ – acrylamide intake from DR)/acrylamide intake from DR × 100. Spearman’s rank correlation coefficients (CC) between DRs and the FFQ were calculated for crude and energy-adjusted values. Energy adjustment was conducted using the residual method. In addition, de-attenuated correlation coefficients were also calculated because the CC between DRs and the FFQ are attenuated by individual variations in variation of DRs, and n is the number of DRs for each participant (28 days). For cross-classification analysis, energy-adjusted acrylamide intake from DRs and the FFQ were divided into five categories by quintile, and the percentage of participants among the same, adjacent, and opposite categories were calculated using both quintile numbers. Moreover, weighted kappa coefficients were calculated. Contribution of each food to total acrylamide intake were calculated as the percentage of acrylamide intake from each food to the total amount of acrylamide intake from DR data. For sensitivity analysis, we conducted the same analysis but excluded acrylamide intake from fried batter. All analyses were performed using SAS (version 9.3, SAS Institute Inc., Cary, NC, USA).

### RESULTS

#### Validity and reproducibility of the FFQ
Mean acrylamide intake from DRs was about 7 µg/day, and the 95th percentile value was 0.23 µg/kg body weight/day (Table 1). About 4% overestimation was observed in Cohort I, and a bare underestimation was observed in Cohort II.

Ranges of energy-adjusted CCs for Cohorts I and II were 0.34 to 0.48 and deattenuated CCs were 0.37 to 0.54 (Table 2). From cross-classification analysis, 26–31% of participants were assigned to the ‘same’ category, 63–74% were assigned to the ‘same and adjacent’ category, and 2–4% were assigned to the ‘extreme’ category. The weighted kappa coefficients were over 0.80. For correlations between FFQs for reproducibility, the range of energy-adjusted CCs were 0.56 to 0.62 for Cohorts I and II.

In the sensitivity analysis, where acrylamide intake from fried batter was excluded, the Spearman’s CCs for crude and energy-adjusted intake were unchanged: Cohort I, r = 0.37 and r = 0.48 in men and r = 0.31 and r = 0.43 in women; Cohort II, r = 0.29 and r = 0.37 in men and r = 0.23 and r = 0.33 in women, respectively.

#### Contribution of each food group to total acrylamide intake from DRs in Japanese people
Beverages, confectioneries, vegetables, potatoes and starches, and cereals contributed to the total acrylamide intake (Table 3). The top five food groups accounted for about 90% of total acrylamide intake. Among all foods, acrylamide from potatoes contributed the most, followed by green teas, and coffees and cocaas. When considering the cooking method of vegetables, sweet peppers, bean sprouts, and onions were contributing foods.

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**Table 1. Comparison of mean acrylamide intake from DR and FFQ**

|                | DR            | FFQ V          | %a  |
|----------------|---------------|----------------|-----|
|                | Mean (SD)     | Median (5th %-ile, 95th %-ile) | Mean (SD)     | Median (5th %-ile, 95th %-ile) |
| **Cohort I**   |               |                |     |
| Crude acrylamide intake (µg/day) |               |                |     |
| Men (n = 102)  | 6.72 (3.70)   | 5.84 (2.94, 13.43) | 6.74 (3.96)   | 6.11 (2.07, 13.10) |
| Women (n = 113)| 6.84 (4.07)   | 6.02 (3.11, 13.15) | 7.30 (4.59)   | 6.36 (3.20, 14.16) |
| All (n = 215)  | 6.78 (3.89)   | 5.92 (2.98, 13.43) | 7.03 (4.30)   | 6.13 (2.16, 13.74) |
| Crude acrylamide intake (µg/body weight/day) |               |                |     |
| Men (n = 102)  | 0.10 (0.06)   | 0.09 (0.04, 0.20) | 0.11 (0.07)   | 0.09 (0.03, 0.20) |
| Women (n = 113)| 0.13 (0.08)   | 0.11 (0.05, 0.24) | 0.14 (0.09)   | 0.12 (0.04, 0.28) |
| All (n = 215)  | 0.12 (0.07)   | 0.10 (0.05, 0.23) | 0.12 (0.08)   | 0.10 (0.03, 0.25) |
| **Cohort II**  |               |                |     |
| Crude acrylamide intake (µg/day) |               |                |     |
| Men (n = 174)  | 7.53 (3.60)   | 6.89 (3.41, 14.80) | 6.94 (3.42)   | 6.37 (2.13, 13.67) |
| Women (n = 176)| 6.97 (3.04)   | 6.39 (3.16, 12.83) | 7.34 (3.34)   | 6.60 (2.63, 13.51) |
| All (n = 350)  | 7.25 (3.33)   | 6.61 (3.34, 14.07) | 7.14 (3.38)   | 6.49 (2.43, 13.64) |
| Crude acrylamide intake (µg/body weight/day) |               |                |     |
| Men (n = 174)  | 0.12 (0.06)   | 0.11 (0.05, 0.23) | 0.11 (0.06)   | 0.10 (0.03, 0.22) |
| Women (n = 176)| 0.13 (0.06)   | 0.12 (0.06, 0.23) | 0.14 (0.06)   | 0.13 (0.05, 0.26) |
| All (n = 350)  | 0.12 (0.06)   | 0.11 (0.06, 0.23) | 0.12 (0.06)   | 0.12 (0.04, 0.25) |

DR, dietary record; FFQ, food frequency questionnaire for validation analysis; SD, standard deviation.

*Percentage differences (%) were calculated from following formula: (“mean FFQ V” − “mean DR”)/“mean DR” × 100.
DISCUSSION

We established an acrylamide database to calculate acrylamide intake for Japanese people and found that 17% of food items in the DRs and 19% of food items in the FFQ were designated as acrylamide-containing foods in the FCT. The deattenuated CC between 28-day DRs and the FFQ for validation was 0.37 to 0.54, weighted kappa coefficients were over 0.80, and energy-adjusted CC between FFQs for reproducibility was 0.56 to 0.62 in both sexes and both cohorts. The main contributing food group based on DR data was beverages, followed by confectioneries, vegetables, potatoes and starches, and cereals.

Our study showed a low-to-moderate correlation between DRs and the FFQ, and kappa coefficients indicated a high degree of coincidence. Moreover, correlations between the two FFQs were moderate. Therefore, acrylamide intake estimated from the FFQ is suitable for analysis as categorical variables in epidemiological studies, particularly for the JPHC prospective cohort study. The European Prospective Investigation into Cancer and Nutrition (EPIC) study reported a crude correlation of 0.35 between DRs and their FFQ.20 Our results are consistent with this previous report.

The mean intake and distribution in our study were similar to the results from the previous Monte Carlo simulation in Japan (mean, 0.166 µg/kg body weight/day; 95th percentile, 0.261 µg/kg body weight/day).7 The percentage difference between DRs and the FFQ in our study was about ±10%, and the distribution was also similar. Hence, we concluded that estimation of dietary

![Table 2. Evaluation of the relationship between DR and FFQ_V and between FFQs by correlation and cross-classification analysis](#)

| Cohort I | \( \text{Crude} \) | \( \text{Energy-adjusted} \) | \( \text{Deattenuated}^d \) | \( \text{Cross-classification}^b \) | \( \text{Weighted } \kappa \text{ coefficient} \) | \( \text{Reproducibility}^e \) |
|-----------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Men (n = 102)** | 0.36 | 0.48 | 0.54 | 31 | 74 | 3 | 0.86 | 0.64 | 0.62 |
| **Women (n = 113)** | 0.30 | 0.42 | 0.48 | 27 | 70 | 4 | 0.85 | 0.62 | 0.56 |
| **Cohort II** | \( \text{Men (n = 174)} \) | 0.29 | 0.37 | 0.40 | 30 | 65 | 3 | 0.84 | 0.65 | 0.61 |
| **Women (n = 176)** | 0.23 | 0.34 | 0.37 | 26 | 63 | 2 | 0.83 | 0.67 | 0.58 |

DR, dietary record; FFQ_V, food frequency questionnaire for validation analysis.

\( ^a \text{Spearman’s correlation coefficients between DRs and the FFQ}_V. \)

\( ^b \text{Percentages were presented based on the cross-classification by quintile between DRs and the FFQ}_V. \)

\( ^c \text{Spearman’s correlation coefficients between two FFQs.} \)

\( ^d \text{Deattenuated CC = Energy-adjusted CC} \times \sqrt{1 + \frac{\lambda}{n}}, \text{where } \lambda \text{ is the ratio of within- to between-individual variance and } n \text{ is number of DRs.} \)

![Table 3. Contribution to total acrylamide intake by food groups from DRs](#)

| Food group number | Food group name | Proportion (%) | Number of assigned foods | Top 5 contributing foods (%) | 1 | 2 | 3 | 4 | 5 |
|-------------------|-----------------|----------------|--------------------------|------------------------------|---|---|---|---|---|
| 16                | Beverages       | 32.1           | 22                       | 18.0                         | 16.3 | 13.8 | 13.2 | 12.9 | 12.7 |
| 15                | Confectioneries | 17.8           | 103                      | 14.3                         | 12.9 | 10.3 | 9.8  | 9.1  | 8.4 |
| 6                 | Vegetables      | 17.6           | 5                        | 15.3                         | 14.0 | 13.6 | 12.9 | 12.2 | 11.8 |
| 2                 | Potatoes and Starches | 14.8           | 2                        | 12.2                         | 11.9 | 11.5 | 11.2 | 10.8 | 10.4 |
| 1                 | Cereals         | 7.9            | 51                       | 8.7                          | 8.2  | 7.7  | 7.2  | 6.9  | 6.3 |
| 5                 | Nuts and Seeds  | 7.9            | 16                       | 8.3                          | 8.0  | 7.4  | 6.9  | 6.5  | 6.2 |
| 17                | Seasonings and Spices | 3.2           | 14                       | 3.5                          | 3.0  | 2.8  | 2.5  | 2.3  | 2.2 |
| 4                 | Pulses          | 0.8            | 6                        | 1.2                          | 1.1  | 0.9  | 0.8  | 0.7  | 0.5 |
| 3                 | Sugars and Sweeteners | 0.8            | 6                        | 0.9                          | 0.8  | 0.7  | 0.6  | 0.5  | 0.4 |
| 7                 | Fruits          | 0.6            | 18                       | 0.7                          | 0.6  | 0.5  | 0.4  | 0.3  | 0.3 |
| 10                | Fishes and Shellfishes | 0.5            | 4                        | 0.5                          | 0.5  | 0.5  | 0.4  | 0.4  | 0.3 |
| 8                 | Mushrooms       | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |
| 9                 | Algae           | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |
| 11                | Meats           | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |
| 12                | Eggs            | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |
| 13                | Milks           | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |
| 14                | Fats and Oils   | 0.0            | 0                        | 0.0                          | 0.0  | 0.0  | 0.0  | 0.0  | 0.0 |

DR, dietary record.
Acrylamide intake from DRs and the FFQ was relatively accurate. On the other hand, the estimated dietary acrylamide intake from Nagata et al’s FFQ is almost three times higher than our estimate. This difference may be partly due to differences in constructing the acrylamide database and calculating acrylamide intake. For example, meat products accounted for 12.4% of the total acrylamide intake in Nagata et al’s report, while no meat-based food items were designated as acrylamide-containing foods and the meat products group accounted for 0% of acrylamide intake in our study. In another example, in contrast to WHO’s report of a measured value for crumbed or battered poultry, we preferentially used a value for fried batter measured in Japan and did not use the value for crumbed or battered poultry to avoid double assessment of acrylamide intake from fried batter. Moreover, we categorized acrylamide intake from fried batter as cereals. These methodological differences may account for the differences in the contribution of the meat group and cereal food group to acrylamide intake. Therefore, differences in mean acrylamide intake levels among studies may be attributed to differences in study criteria and calculation methods used.

Our results indicate that acrylamide intake by Japanese people is about one tenth of that estimated by JECFA (1 µg/kg body weight/day for the general population). Moreover, the acrylamide intake of Japanese people is about a quarter of that of the Dutch population (0.45 µg/kg body weight/day), which corresponds to the amount of acrylamide derived only from potato crisps among the Dutch. These results suggest that acrylamide intake by Japanese people is much lower than that of western populations. However, a previous study reported that the margin of exposure is less than 10,000 when the benchmark dose lower confidence limit is 0.31 mg/kg body weight/day for mammary tumors in rats. Therefore, the Food Safety Commission of Japan calls for vigilance regarding the possibility of a carcinogenic effect of dietary acrylamide. Further, the results of epidemiological studies from western countries are inconsistent. Hence, epidemiological studies should be conducted to clarify the risk of dietary acrylamide intake on carcinogenicity in the Japanese population.

We found that acrylamide intake from vegetables accounted for a proportion of the total acrylamide intake, a finding which is consistent with previous reports in Japan. Contributing foods in western countries are primarily potato-based foods (eg, fried potato), wheat-based products (eg, biscuits), and coffee, but not vegetables. Therefore, cooked vegetables are an important source of acrylamide intake, at least in the Japanese population.

In our study, coffee, green tea, and vegetables accounted for about half of the total acrylamide intake. These foods are often reported to have preventive effects on cancers. Hence, an association analysis between acrylamide intake and cancers in the Japanese population is warranted and is likely to differ from the results from western countries.

The main strength of this study was the use of 28-day weighted DRs to calculate acrylamide intake. The use of 28-day records allowed us to better estimate the association between acrylamide intake and contributing foods from DRs than previous studies.

There are several limitations of this study. First, acrylamide intake from DRs and the FFQ may have been underestimated because the list of acrylamide-containing foods covered only about 17–19% of food items from each FCT. However, we considered home cooking methods for specific foods (mostly vegetables) and found that the contribution of vegetables was relatively high. This result indicates that cooking methods are important for estimating acrylamide intake. Second, we could not validate the calculated acrylamide intake from DRs. As acrylamide concentration varies even within the same food product depending on the cooking temperature and time, we used median or mean values of measurements to reduce the effect of such variations. Therefore, a validation study using duplicate methods is needed to clarify the accuracy of calculating acrylamide intake from DRs. Third, we could not compare dietary acrylamide intake and biomarkers, such as hemoglobin adduct concentrations of acrylamide and glycidamide. The Nurses’ Health Study II reported a moderate correlation between dietary acrylamide intake and hemoglobin adduct concentrations. However, dietary acrylamide levels are affected by individuals’ metabolism and lifestyle, causing sensitivity to dietary acrylamide to vary. This was reflected in the EPIC study, where, although acrylamide intake from the FFQ was correlated with that from DRs, the correlation between acrylamide intake from the FFQ and hemoglobin adduct concentrations was low.

Therefore, analysis using biomarkers is needed to understand dietary acrylamide exposure in Japanese people.

The validity of estimating acrylamide intake using a FFQ was low to moderate in this study. However, the high validity of categorization suggests that the FFQ is suitable for use in epidemiological studies, particularly for the JPHC prospective cohort study. Further, the contributing foods to total acrylamide intake in the Japanese population were different from those in western countries, possibly due to differences in home food preparation methods. Therefore, considering household cooking methods, especially for vegetables, is important for assessing the acrylamide intake level in Japanese people.

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Author contribution: JI and TS designed the study; ST, TS, JI, NS, and MI arranged the field survey; AK and MN contributed to the data cleaning; AK performed the statistical analysis, interpreted the results and wrote the manuscript; and all authors reviewed the manuscript and contributed to the discussion. The investigators and their affiliations in the validation study of the self-administered FFQ in the JPHC Study (the JPHC FFQ Validation Study Group) at the time of the study were listed in the website (http://epi.ncc.go.jp/en/jphc/781/7952.html).

Conflicts of interest: None declared.

**REFERENCES**

1. Food Safety Commission of Japan. Evaluation document of dietary acrylamide produced by heating. Available from: https://www.fsc.go.jp/osirase/acrylamide1/data/acrylamide_hyokasyo1.pdf (Accessed in 1/17/2017).

2. IARC working group on the evaluation of carcinogenic risks to humans: some industrial chemicals. Lyon, 15–22 February 1994. IARC Monogr Eval Carcinog. Risks Hum. 1994;60:1–560.

3. Tareke E, Rydberg P, Karlsson P, Eriksson S, Törnqvist M. Analysis...
of acrylamide, a carcinogen formed in heated foodstuffs. J Agric Food Chem. 2002;50:4996–5006.

4. Granby K, Nielsen NJ, Hedegaard RV, Christensen T, Kann M, Skibsted LH. Acrylamide-asparagine relationship in baked/toasted wheat and rye breads. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2008;25:921–929.

5. Konings EJ, Hogervorst JG, van Rooij L, et al. Validation of a database on acrylamide for use in epidemiological studies. Eur J Clin Nutr. 2010;64:534–540.

6. Freisling H, Moskal A, Ferrari P, et al. Dietary acrylamide intake of adults in the European Prospective Investigation into Cancer and Nutrition differs greatly according to geographical region. Eur J Nutr. 2015;52:1369–1380.

7. Food Safety Commission of Japan. Study on estimate of acrylamide intake from food; interim report. Available from: https://www.fsc.go.jp/fsctis/technicalResearch/show/cho99920151507 (Accessed in 07/01/2016).

8. Ishihara J, Inoue M, Kobayashi M, et al; JPHC FFQ Validation Study Group. Impact of the revision of a nutrient database on the validity of a self-administered food frequency questionnaire (FFQ). J Epidemiol. 2006;16:107–116.

9. Tsugane S, Sasaki S, Kobayashi M, Tsubono Y, Akabane M; JPHC. Validity and reproducibility of the self-administered food frequency questionnaire in the JPHC Study Cohort I: study design, conduct and participant profiles. J Epidemiol. 2003;13(1)(Suppl):S2–S12.

10. Ishihara J, Sobue T, Yamamoto S, et al; JPHC. Validity and reproducibility of a self-administered food frequency questionnaire in the JPHC Study Cohort II: study design, participant profile and results in comparison with Cohort I. J Epidemiol. 2003;13(1)(Suppl):S134–S147.

11. National Institute for Environmental Studies, Japan. Study on statistical estimate of acrylamide intake from foods.

12. Ministry of Agriculture, Forestry and Fisheries. Risk profile sheet relating to the food safety; for acrylamide. Available from: http://www.maff.go.jp/j/syousei/ezaisaku/risk/analysis/priority/pdf/150807,rp.aa.pdf (Accessed in 07/01/2016).

13. National Institute of Health Sciences. Acrylamide analysis in food. Available from: http://www.mhlw.go.jp/topics/2002/11/tpl1101-1a.html (Accessed in 07/01/2016).

14. Mizukami Y, Kohta K, Yamaguchi Y, et al. Analysis of acrylamide in green tea by gas chromatography-mass spectrometry. J Agric Food Chem. 2006;54:7370–7377.

15. Takatsuki S, Nemoto S, Sasaki K, Maitani T. Production of acrylamide in agricultural products by cooking. Shokuhin Eiseigaku Zasshi. 2004;44:44–48.

16. Yoshida M, Ono H, Ohnishi-Kameyama M, et al. Determination of acrylamide in processed foodstuffs in Japan. Nippon Shokuhin Kagaku Kagaku Kaishi. 2011;58:525–530.

17. Food Safety Commission of Japan. Information clearing sheet for Acrylamide. Available from: https://www.fsc.go.jp/fsctis/attachedFile/download?retrievalId=kai20111222sfc&fileId=520 (Accessed in 07/01/2016).

18. FAO/WHO. Health implications of Acrylamide in Food. Available from: http://www.who.int/foodsafety/publications/acrylamide-food/en/ (Accessed in 07/01/2016).

19. Ferrari P, Freisling H, Duell EJ, et al. Challenges in estimating the validity of dietary acrylamide measurements. Eur J Nutr. 2013;52:1503–1512.

20. Nagata C, Konishi K, Tamura T, et al. Associations of acrylamide intake with circulating levels of sex hormones and prolactin in premenopausal Japanese women. Cancer Epidemiol Biomarkers Prev. 2015;24:249–254.

21. Joint FAO/WHO Expert Committee on Food Additives (JECFA). Seventy-Second meeting, Rome, 16–25 February 2010, Summary and Conclusions (JECFA/72/SC). Available from: http://www.who.int/foodsafety/chem/summary72.rev.pdf (Accessed in 12/27/2016).

22. Food Safety Commission of Japan. Risk Assessment Report of dietary acrylamide. Available from: https://www.fsc.go.jp/otisuse/acrylamide1.data/acrylamide_hyokasyo1.pdf (Accessed in 12/27/2016).

23. Pelucchi C, Bosetti C, Galeone C, La Vecchia C. Dietary acrylamide intake and cancer risk: an updated meta-analysis. Int J Cancer. 2015;136:2912–2922.

24. Dybing E, Sanner T. Risk assessment of acrylamide in foods. Toxicol Sci. 2003;73:7–15.

25. Wilson KM, Mucci LA, Rosner BA, Willett WC. A prospective study on dietary acrylamide intake and the risk for breast, endometrial, and ovarian cancers. Cancer Epidemiol Biomarkers Prev. 2010;19:2503–2515.

26. Miyakoshi T, Sobue T, Kitaamura T, et al. Association between green tea/coffee consumption and biliary tract cancer: a population-based cohort study in Japan. Cancer Sci. 2016;107:76–83.

27. Kurahashi N, Sasazuki S, Iwasaki M, Inoue M, Tsugane S; JPHC Study Group. Green tea consumption and prostate cancer risk in Japanese men: a prospective study. Am J Epidemiol. 2008;167:71–77.

28. Shimazu T, Inoue M, Sasazuki S, et al; JPHC Study Group Members of the Japan Public Health Center-based Prospective Study. Coffee consumption and risk of endometrial cancer: a prospective study in Japan. Int J Cancer. 2008;123:2406–2410.

29. Kurahashi N, Sasazuki S, Iwasaki M, Inoue M, Tsugane S; JPHC Study Group. Green tea consumption and prostate cancer risk in Japanese men: a prospective study. Am J Epidemiol. 2008;167:71–77.