Consumption of sodium and salted foods in relation to cancer and cardiovascular disease: the Japan Public Health Center–based Prospective Study1–4

Ribeka Takachi, Manami Inoue, Taichi Shimazu, Shizuka Sasazuki, Junko Ishitohara, Norie Sawada, Taiaki Yamaci, Motoki Iwasaki, Hiroyasu Ito, Yoshitaka Tsubono, and Shoichiro Tsugane for the Japan Public Health Center–based Prospective Study Group

ABSTRACT
Background: Although the influence of salt, per se, on the risk of cancer or cardiovascular disease (CVD) might differ from that of salt-preserved foods, few studies have simultaneously examined the effects of sodium and salted foods on the risk of either cancer or CVD.

Objective: We simultaneously examined associations between sodium and salted food consumption and the risk of cancer and CVD.

Design: During 1995–1998, a validated food-frequency questionnaire was administered to 77,500 men and women aged 45–74 y. During up to 598,763 person-years of follow-up until the end of 2004, 4476 cases of cancer and 2066 cases of CVD were identified.

Results: Higher consumption of sodium was associated with a higher risk of CVD but not with the risk of total cancer: multivariate hazard ratios for the highest compared with lowest quintiles of intake were 1.19 (95% CI: 1.01, 1.40; P for trend: 0.06) for CVD and 1.04 (95% CI: 0.93, 1.16; P for trend: 0.63) for total cancer. Higher consumption of salted fish roe was associated with higher risk of total cancer, and higher consumption of cooking and table salt was associated with higher risk of CVD. Similar results were seen for the risk of gastric or colorectal cancer and stroke.

Conclusions: Sodium intake as a whole salt equivalent may not increase the risk of cancer but may increase that of CVD. In contrast, salted food intake may increase the risk of cancer. Our findings support the notion that sodium and salted foods have differential influences on the development of cancer and CVD.

INTRODUCTION
Cancer and cardiovascular disease (CVD) are the leading causes of death in many parts of the world. Salt or processed foods with high salt concentrations or preservative content have been identified as risk factors for some cancers (1) and CVD (2). In previous observational studies, however, exposure from the consumption of salt as a whole might have been distinct from that of salt-preserved foods, which is explained as follows. Because the contribution of the salty seasonings used in cooking or at the table to sodium chloride intake was relatively small, the previous studies might have been unable to discern a difference between salt per se and salted food in their effect on these diseases. If so, any effect of salt on gastric cancer may have resulted primarily from the regular consumption of highly salt-concentrated preserved foods, rather than from total sodium chloride (1, 3). Furthermore, salt-preserved foods contain both potentially disadvantageous (eg, N-nitroso compounds) and advantageous factors [eg, n–3 (omega-3) polyunsaturated fatty acids, potassium, or antioxidants (1, 2, 4, 5)]. Despite these possible differences in the effect of salt-preserved foods and of total sodium from salty seasonings and salt-preserved foods on the risk of total cancer and CVD, most studies to date have evaluated sodium or salted food consumption in relation to the risk of site-specific cancer or CVD separately.

One approach to determine the effect of salt consumption as a whole sodium chloride equivalent or as salted food consumption on disease risk is to examine their associations with the risk of cancer and CVD simultaneously in the same population. To our knowledge, however, no such prospective cohort study has been reported. Because of the difficulty of estimating habitual salt or sodium intake, few studies have simultaneously examined the effects of sodium and salted foods on the risk of either cancers [2 studies for gastric cancer (6, 7)] or CVD [7 studies, for sodium only (8–14)]. Asian populations tend to differ from Western populations with respect to the distribution of exposure (higher

1 From the Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo, Japan (RT, MI, TS, SS, NS, TY, MI, and ST); the Division of Clinical Epidemiology, Tohoku University Graduate School of Medicine, Miyagi, Japan (RT and YT); the Department of Nutrition, Junior College of Tokyo University of Agriculture, Tokyo, Japan (HI); the Public Health Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine, Osaka, Japan (HI); and the Division of Health Policy, Tohoku University School of Public Policy, Miyagi, Japan (YT).

2 The funding agencies had no role in the research presented herein, and the researchers were fully independent in pursuing this research.

3 Supported by the Grants-in-Aid for Cancer Research and for the Third-Term Comprehensive 10-year Strategy for Cancer Control from the Ministry of Health, Labor, and Welfare of Japan.

4 Address correspondence to M Inoue, Epidemiology and Prevention Division, Research Center for Cancer Prevention and Screening, National Cancer Center, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan. E-mail: mmminoue@ncc.go.jp.

Received August 30, 2009. Accepted for publication November 18, 2009.

consumption of sodium and salt-preserved fish) and outcomes (higher incidence of gastric cancer and stroke). Moreover, the contribution of salty seasonings used in cooking or at the table to total salt intake (excluding miso) is relatively high, at 52% in Japan (15). Studies that aim to characterize the influence of sodium and salted food consumption on the risk of cancer and CVD in Asian populations are therefore important.

In this study, we used a validated, comprehensive food-frequency questionnaire (FFQ) with estimation of habitual cooking and table salt to examine associations between sodium and salted foods and the risk of cancer and CVD in a population-based prospective cohort study in Japan. Particular focus was placed on the intake of sodium and specific salt-preserved foods.

SUBJECTS AND METHODS

Study population

The Japan Public Health Center–based Prospective Study was conducted in 2 cohorts, one initiated in 1990 (cohort I) and the other in 1993 (cohort II). The study design has been described in detail previously (16). The study protocol was approved by the Institutional Review Board of the National Cancer Center, Tokyo, Japan.

The study population was defined as all registered Japanese inhabitants in 11 public health center areas, aged 40–59 y in cohort I and aged 40–69 y in cohort II, who were identified by the population registries maintained by the local municipalities. Two public health center areas (Tokyo and Osaka) were excluded from the present analysis because either cancer or CVD incidence data, or both, were not available.

Surveys of the cohort participants by self-administered questionnaire were conducted twice, the first in 1990 (cohort I) and 1993 (cohort II), and the second in 1995 (cohort I) and 1998 (cohort II). Because the second survey included more comprehensive information on food intake frequency than the first, the second survey was used as the starting point to assess dietary exposure in the present study. The questionnaire also included information on medical history and lifestyle factors, such as smoking and alcohol drinking.

After the exclusion of 9272 persons who had died, moved out of a study area, or were lost to follow-up before the starting point, the 107,400 subjects who remained were eligible for participation. Of these, 91,225 subjects responded (42,761 men and 48,464 women; response rate 84.9%) and were included in the present study.

Food-frequency questionnaire

The FFQ asked about the usual consumption of 138 foods and beverages, which included 4 seasonings (dressing, mayonnaise, Worcestershire sauce, and ketchup), during the previous year in each food consumed (g/d) was calculated from the responses. Energy and nutrient intake, including sodium, were calculated with the use of the Standardized Tables of Food Composition, fifth revised edition (18). Sodium intake from cooking salt and soy sauce was estimated for 3 food groups (meats, fish, and vegetables) from the responses for dietary and cooking behaviors, with cooking salt for 6 cooking methods (raw, stewed, grilled, deep-fried, stir-fried, and other) that have specified salt content (0.8–1.5%) multiplied by the individual intake of each food group according to the cooking methods most frequently used by the individual. In addition, table salt and soy sauce added to these food groups were taken into account for sodium intake according to specified salt content (0–0.5%) for the 3 frequency categories (19). Miso soup consumption was calculated with the use of 6 frequency categories and 9 categories for the number of bowls per day, which ranged from <1 to ≥10 bowls/d, and was further adjusted for taste preference by multiplying by the specified coefficient for mild, common, and strong taste preferences of 0.75, 1.0, and 1.3, respectively.

The following food items were considered as salted foods in our analysis: pickled vegetables (6 items: Chinese radishes, green leafy vegetables, plums, Chinese cabbage, cucumbers, and eggplant; 1.5–7.6% salt content); dried and salted fish (3 items: salted fish (salted codfish or atka mackerel or salmon); himono (dried and salted Japanese horse mackerel); shirasuboshi (dried young sardines); 1.7–4.1%); salted fish roe [one item included 2 descriptions: tarako (salted Alaska pollack roe) or suziko (salted salmon roe); 4.6–4.8%]; and miso soup (1%). Salt content data for specific food items other than miso soup were taken from the Standardized Tables of Food Composition, fifth revised edition (18). The weighting ratios for miso soup composition, which consists of miso and cooking water, were 8% and 92%, respectively, and were obtained from the dietary records (19).

The validity of the FFQ for the assessment of sodium intake has been confirmed (20). Spearman’s correlation coefficients between energy-adjusted sodium intake based on the FFQ and those based on 28-d (or 14-d for the Ishikawa public health center area) dietary records among subsamples (n = 215 and 350 for cohorts I and II, respectively) of men and women were 0.47 and 0.50 for cohort I and 0.32 and 0.31 for cohort II, respectively. Correlation coefficients for the reproducibility of the FFQ administered 1 y apart for men and women were 0.49 and 0.63 for cohort I and 0.56 and 0.67 for cohort II, respectively (21, 22). To examine the accuracy of habitual sodium intake based on the FFQ over an extended period, correlation coefficients between energy-adjusted sodium concentration based on the FFQ and creatinine-adjusted sodium concentrations based on 2 measurements of 24-h urinary excretion at a 7-mo interval for men and women were 0.42 and 0.30, respectively, among subsamples of cohort I (20).

Follow-up

Subjects were followed from the starting point until 31 December 2004. Changes in residence status, including survival, were obtained annually from the residential registry in each area or, for those who had moved out of the study area, through the municipal office in the area to which they had moved. Mortality data for persons in the residential registry are forwarded to the Ministry of Health, Labor and Welfare and are coded for inclusion in the national Vital Statistics. Residency registration and death registration are required by the Basic Residential Register Law and Family Registry Law, respectively, and the registries are thought to be complete. During the follow-up period in the
The occurrence of cancer was identified by active patient notification from major local hospitals in the study area and from data linkage with population-based cancer registries, with permission from the local governments responsible for the cancer registries. Cancer cases were coded in accordance with the International Classification of Diseases for Oncology, third edition (23). In our cancer registry system, the proportion of cases for which information was available from death certificates only was 5.0%. Diagnoses of myocardial infarction according to the criteria of the MONICA (Monitoring Trends and Determinants of Cardiovascular Disease) project (24) and diagnoses of stroke according to the criteria of the National Survey of Stroke (25) were confirmed for all cases by either or both computer tomographic scan and magnetic resonance imaging as recorded in the medical record and reviewed by hospital or public health center physicians in each registered major local hospital in each public health center area (26, 27). CVD cases with a death certificate or self-report only, without confirmation by medical records, were treated as non-CVD cases. CVD was defined as myocardial infarction or stroke, whichever occurred first. We confirmed 7056 cases of newly diagnosed cancers and 3349 cases of CVD among the 91,225 subject by 31 December 2004.

Statistical analysis

Of the 91,225 respondents, we excluded subjects with a history of cancer or coronary heart disease or stroke (n = 8,165) and those who did not complete the diet component of the questionnaire (n = 1482). Subjects with a history of these conditions were defined as diagnosed with cancer or CVD before the starting point or from self-reports in the questionnaire. Of the 81,578 subjects, 4078 who reported extreme total energy intake (lower and upper 2.5 percentiles: 910 and 4000 kcal/d, respectively) were excluded, which left 77,500 subjects (35,730 men, 41,770 women) for final analysis, including 4476 with CVD (1745 stroke, 338 myocardial infarction). Participants with both cancer and CVD were included in both analyses. We performed separate analyses for major site-specific cancers (gastric, colorectal, or lung cancer: 50% of total cancer cases) and stroke or myocardial infarction. Of the CVD cases, participants with both stroke and myocardial infarction were included in both analyses.

Person-years of follow-up were calculated for each subject from the starting point to the date of diagnosis, date of emigration from the study area, date of death, or end of the follow-up period (31 December 2004), whichever occurred first. Subjects lost to follow-up were censored at the last confirmed date of presence in the study area. A total of 593,620 person-years were accrued for the cancer analysis and 598,763 for the CVD analysis.

Hazard ratios (HRs) and 95% CIs were calculated for the categories of energy-adjusted sodium and salted food consumption in quintiles for men and women combined, with the lowest consumption category as the reference, with the use of Cox proportional hazards models with adjustment for potential confounding variables according to the SAS PHREG procedure (SAS software, version 9.1; SAS Institute Inc, Cary, NC). A residual model was used for energy adjustment of sodium and salted food consumption (28).

We conducted the initial analyses by adjusting for sex and age at the starting point (5-y groups). In the multivariate model, we further adjusted for body mass index (BMI; in kg/m²) (<19, 19–22.9, 23–24.9, 25–26.9, and ≥27), smoking status (never, past, and current), alcohol consumption (none, occasional, or 1–149, 150–299, 300–449, and ≥450 g ethanol/wk), physical activity in metabolic equivalent task-hours/d (<30, 30–34.9, 35–39.9, and ≥40), and quintiles of total energy, potassium (as a proxy for the intake of fruit and vegetables for the analysis of cancers) and calcium intake (29, 30). We did not adjust for area in the models, because salt or salted food consumption was substantially defined by area, and adjustment may therefore have masked the true influence of salt or salted food on gastric cancer or stroke, which accounted for the largest part of total cancer (19.5%) and CVD (84.5%), respectively (31–34). Subjects for whom values for any of the potential confounders were missing were excluded from the multivariate analysis (7079 were excluded, which left 70,421 in the analyses), because findings did not materially differ when subjects with missing values were retained in the analyses by assigning dummy variables for missing responses. We also assessed linear associations with the use of the median values of sodium or salted food intake for each quintile.

Because the distribution of sodium consumption differed by sex, we also performed a stratified analysis according to sex-specific quintile of sodium or salted food consumption. We additionally performed subgroup analyses according to smoking status (“never” as nonsmoker or “past” and “current smoker” as ever smoker), age (<60 or ≥60 y), cohort (I or II), BMI (<25 or ≥25), and alcohol intake (<300 or ≥300 g ethanol/wk). All P values were 2-sided, and statistical significance was determined at P < 0.05.

RESULTS

Contributions to gross sodium intake in this population from pickled vegetables, dried and salted fish, salted fish roe, miso soup, and cooking and table salt were 11.1%, 3.4%, 0.7%, 18.8%, and 38.8%, respectively, and the correlation coefficients between sodium and these foods were 0.46, 0.24, 0.18, 0.43, and 0.71, respectively. Sodium intake ranged from a median value of 3084 mg/d in the lowest quintile to 6844 mg/d in the highest. Subjects with higher sodium consumption were slightly older.

Age-adjusted values for subject characteristics according to quintile of sodium consumption are shown in Table 1. Subjects with higher consumption were less likely to be men, drinkers, and ever smokers, and more likely to consume higher amounts of potassium and calcium. Higher sodium intake was not associated with levels of physical activity or prevalence of ever smoking or overweight.

Whereas no association was shown between sodium or cooking and table salt consumption and cancer, higher consumption of salted fish roe was significantly associated with a higher risk of total cancer, as shown in Table 2. Furthermore, the HR of total cancer was significantly higher for the highest quintile of dried and salted fish than the lowest, albeit without a linear trend. A significant positive association was shown between sodium consumption and risk of CVD, as well as...
between cooking and table salt and CVD, whereas no positive association was shown between any specific salted food item and risk of CVD. On the contrary, an inverse association was shown between dried and salted fish and CVD risk.

On additional analysis that used major site-specific cancers (gastric and colorectal cancer) and stroke or myocardial infarction as endpoints (Table 3), higher consumption of pickled vegetables was associated with a higher risk of gastric cancer, whereas higher consumption of dried and salted fish and salted fish roe was associated with a higher risk of both gastric cancer and colorectal cancer (although the linear trend was not significant for gastric cancer risk according to dried and salted fish intake). In contrast, no association was shown between sodium or cooking and table salt consumption and any major site-specific cancer, including gastric cancer. A significant positive association was shown between sodium consumption as well as cooking and table salt intake and risk of any major site-specific cancer, including breast cancer. A significant positive association was shown between sodium, or any salted food intake for the risk of cancers or CVDs (data not shown). The results did not materially differ in those obtained with sex-combined quintiles. Specifically, no association was shown between sodium consumption and risk of total cancer for either sex, with HRs that corresponded for the highest compared with lowest quintiles of intake of 1.11 (95% CI: 0.96, 1.28; P for trend: 0.23) and 0.94 (95% CI: 0.79, 1.11; P for trend: 0.45) for men and women, respectively. Higher consumption of salted fish roe among women and pickled vegetables among men and women was nonsignificantly associated with a higher risk of total cancer (data not shown). CVD risk was positively but nonsignificantly associated with sodium consumption for both men (HR: 1.18, 95% CI: 0.96, 1.45; P for trend: 0.08) as well as with cooking and table salt consumption (data not shown). The only salted food positively associated with CVD risk among women was salted fish roe. On the contrary, higher consumption of dried and salted fish was associated with lower risk of CVD among men (data not shown). Tests of interaction were not statistically significant between sex and sodium, or any salted food intake for the risk of cancers or CVDs (data not shown). The results did not materially differ in analyses stratified by smoking status, age, cohort, BMI, or alcohol intake (data not shown).

We also conducted analyses that excluded subjects who reported medication use for hypertension, diabetes, or hyperlipidemia.
Although the results for total cancer and major site-specific cancers were not substantially changed (data not shown), multivariate HRs of CVD and stroke for the highest compared with lowest quintiles of sodium intake were greater than those before the exclusion of these patients (HR for CVD: 1.30, 95% CI: 1.06, 1.60; $P$ for trend: < 0.01; HR for stroke: 1.36, 95% CI: 1.09, 1.71; $P$ for trend < 0.01).

### DISCUSSION

In this population-based prospective cohort study in Japan, we observed that higher consumption of sodium as a whole was associated with an increased risk of CVD but not of cancer. In contrast, higher consumption of salted fish was associated with a higher risk of cancer but not of CVD. Moreover, higher consumption of dried and salted fish was associated with a lower risk of CVD and stroke compared to the lowest intake. The risk of CVD and stroke increased with increasing sodium intake, as evidenced by the observed trends.
risk of CVD. To our knowledge, this is the first prospective cohort study to simultaneously examine associations between sodium and salted foods and the risk of cancer and CVD.

Results from 7 previous prospective cohort studies that examined the association between sodium intake and CVD risk have been poorly consistent: 3 studies showed significant associations between sodium and risk (8, 9, 11), 1 showed a significant inverse association (12), and 3 showed no association (10, 13, 14). These studies used different methods to assess exposure: 2 used 24-h urinary sodium excretion (9, 10), 1 used a validated FFQ that consisted of 35 items (8), and 4 used a single 24-h dietary recall method (11–14). Our results are consistent with 2 of the 3 studies that used an FFQ or 24-h urinary excretion to assess habitual salt intake (8, 10).

Only one previous study has examined the association between salted foods and total cancer risk (35), although at a small scale (155 cases). Results showed no association between consumption of salted fish, Japanese pickles, and miso soup with total sodium, salted, and salted foods and the risk of cancer and CVD.
cancer mortality. With regard to gastric cancer, the 6 prospective studies of the association of this cancer with total salt intake after adjustment for other risk factors (6, 7, 36–39) were inconsistent, although the report of a joint World Cancer Research Fund/American Institute for Cancer Research Expert Consultation identified salt as a "probable" risk of gastric cancer (1): 2 of 3 studies conducted in Japan showed a positive association between salt intake and gastric cancer incidence (6, 38) and 3 conducted in Western countries [Norway (7), Netherlands (37), and the United States (39)] showed no association, whereas the third study conducted in Japan reported an inverse association between total salt intake and gastric cancer mortality. Of these studies, one conducted in the Japan Public Health Center–based cohort reported positive associations with the risk of gastric cancer for both salt intake and salted foods but did not take table salt or cooking method into consideration when total salt intake was calculated (6). In contrast, the present study did include table salt or cooking method variables, which correlated strongly with total sodium intake ($r = 0.71$), and showed them to represent 40% of total sodium intake. Nevertheless, we observed no association between total sodium consumption and the risk of either total cancer or gastric cancer.

The major strength of the present study was its prospective design, which avoided exposure recall bias. Other strengths included the following: study subjects were defined as the general population; response rate to the questionnaire (85%) was acceptable for study settings such as this; and the proportion of losses to follow-up (0.02%) was negligible. Furthermore, the use of a general population in Asia and an FFQ enabled sodium intake to be estimated from not only salted foods but also salty seasonings from dietary and cooking behaviors, which likely represented a relatively large portion of sodium intake. In the present study, this strength may have eliminated the possibility that the observed absence of an association between sodium intake as a whole salt equivalent and gastric cancer incidence was attributable to any inability to take into account salty seasonings from dietary and cooking behaviors in the estimation of total sodium intake.

The present results suggest that the associations of cancer with specific foods with high salt concentrations, such as salted fish roe, are not due to the amount of salt per se, but rather to other causes. Consistent with our results, Tsugane et al (6) reported that, after adjustment for total salt intake, higher consumption of salted fish roe among men and women and of dried or salted fish among men was associated with a higher risk of gastric cancer. One potential explanation for this may have been the presence of chemical carcinogens such as N-nitroso compounds in dried fish or salted fish roe, which can be formed by the reaction of nitrate or nitrite in the curing process or in the body (1, 4, 5), or heterocyclic amines, which have been detected in fish or meat cooked in high temperatures, such as grilling (40), which is commonly used for dried and salted fish in Japan. An additional, inseparable explanation is the destruction of the gastric mucosal barrier by a high intragastric salt concentration, which leads to inflammation, diffuse erosion, and degeneration. The subsequent proliferative change may exacerbate the effect of food-derived carcinogens (3, 41). In contrast, the decreased risk of CVD with dried and salted fish intake might reflect beneficial cardiovascular effects of n–3 polyunsaturated fatty acids in fish in the inhibition of platelet aggregation, modulation of the inflammatory system, and lowering of blood pressure (27). Salted foods might thus not be as precise a surrogate marker of total salt in the investigation of the influence on cancer and CVD as whole sodium chloride consumption.

Our study has several potential limitations. First, with the use of multiple 24-h urinary sodium excretion as a reference, the validity of the FFQ for sodium intake was moderate at best [$r = 0.30–0.42$ (20)]. Some misclassification in the FFQ was unavoidable, and it is possible that the accuracy of salt intake was less than that of salted food intake (6). If this biased the association between sodium and cancers toward the null, then the observed association would have underestimated the true magnitude of the association between sodium and CVD as well as cancers. Second, variation in sodium consumption among subjects was also moderate at best, with median intake in the highest quintile group (6844 mg) only 2.2-fold that in the lowest (3084 mg; Table 1). However, this range was similar to that of a study based on 24-h urinary excretion, which identified positive associations between sodium intake and CVD [1.6-fold difference (9)]. Given that this variation was sufficient to detect an association between sodium intake and CVD risk, the possibility that the lack of association between sodium intake and total and gastric cancer was due to insufficient variation therefore appears unlikely. In addition, we did not obtain information on infection with Helicobacter pylori, a strong risk factor for gastric cancer (42). Because salted food intake may increase the risk of $H. pylori$ infection, the prevalence of infection would have been higher in subjects with higher intakes of salt or salted food (43). Therefore, even if $H. pylori$ infection causes gastric cancer, we believe it unlikely that the failure to account for $H. pylori$ infection masked a positive association between the consumption of sodium and the risk of gastric cancer.

In conclusion, this population-based prospective cohort study in Japan showed that the amount of sodium as a whole salt equivalent was not associated with the risk of cancer but was associated with an increased risk of CVD. In contrast, the intake of highly salt-concentrated preserved foods may increase the risk of cancer. Our findings support the notion that sodium and salted foods have differential influences on the development of cancer and CVD.

Members of the Japan Public Health Center–based Prospective Study Group (principal investigator: S Tsugane): S Tsugane, M Inoue, T Sobue, and T Hanaska (Research Center for Cancer Prevention and Screening, National Cancer Center, Tokyo); J Oguta, S Baba, T Mannami, A Okayama, and Y Kokuho (National Cardiovascular Center, Suita); K Miyakawa, F Saito, A Koizumi, Y Sano, I Hashimoto, T Ikuta, and Y Tanba (Iwate Prefectural Ninohe Public Health Center, Ninohe); Y Miyajima, N Suzuki, S Nagasawa, Y Furusugi, and N Nagai (Akitaka Prefectural Yokote Public Health Center, Yokote); H Sanada, Y Hatayama, F Kobayashi, U Huchino, Y Shirai, T Kondo, R Sasaki, Y Watanabe, Y Miyagawa, and Y Kobayashi (Nagano Prefectural Saku Public Health Center, Saku); Y Kishimoto, E Takara, T Fukuyama, M Kinjo, M Irie, and H Sakiyama (Okinawa Prefectural Chubu Public Health Center, Okinawa); K Imoto, H Yazawa, T Seo, A Seiko, F Ito, F Shoji, and R Saito (Katsushika Public Health Center, Tokyo); A Murata, K Minato, K Motegi, and T Fujiieda (Ibaraki Prefectural Mito Public Health Center, Mito); T Abe, M Katagiri, M Suzuki, and K Matsui (Niigata Prefectural Kashiwazaki and Nagaoka Public Health Center, Kashiwazaki and Nagaoka); M Doi, A Terao, Y Ishikawa, and T Tagami (Kochi Prefectural Chuo-higashi Public Health Center, Tosayamada); H Doi, M Urata, N Okamoto, F Ide, and H Suetaw (Nagasaki Prefectural Kamigoto Public Health Center, Arikawa);
REFERENCES


