



# Modification of Dietary Habits for Prevention of Gout in Japanese People: Gout and Micronutrient Intake or Alcohol Consumption

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**Abstract:** In Japan, most of gout patients are adults, and the prevalence of gout has increased markedly since the 1960s. This phenomenon is thought to be attributed to the westernization of the Japanese diet since 1955. Monitoring the intake of nutrients and foods in Japanese people is essential in the prevention of gout. The objective of this article is to propose a preventive method for gout through the evaluation of recent dietary habits in Japanese people. In this article, the author suggests the importance of micronutrient (vitamin and mineral) intake and alcohol consumption for prevention of gout in Japanese people referencing the results of clinical research reported. The author used the data of the Comprehensive Survey of Living Conditions in Japan for the number of gout patients (1986-2016) and the data of the National Health and Nutrition Survey in Japan (1946-2017) for the intake of micronutrients. The relationship between the number of gout patients and micronutrient intake in Japanese people was examined. Modification of micronutrient intake for the prevention of gout in Japanese people (especially adults) is suggested as follows: limiting or decreasing salt intake; increase intake of vitamin A, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, calcium, potassium, magnesium, and zinc; and limiting alcohol consumption.

**Keywords:** Alcohol, Dietary Habits, Gout, Hyperuricemia, Mineral, Uric Acid, Vitamin

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## 1. Introduction

The phenomenon that the number of gout patients has increased with the westernization of the Japanese diet since 1955 has been described in the previous report [1]. Koguchi [2] has suggested modification of macronutrient intake for the prevention of gout in Japanese people (especially adults) as follows: energy-providing nutrient balance (percentages of proteins, fats, and carbohydrates in total energy intake) should be within the range of the tentative dietary goal for preventing lifestyle-related diseases (DG); reduce fat (especially animal fat) intake and maintain the mean ratio of energy intake from saturated fatty acids in total energy intake (Saturated fatty acids/Energy) within the range of the tentative dietary goal for preventing lifestyle-related diseases (DG); limiting or decreasing intake of fat (especially animal fat); replacement of saturated fatty acids (e.g., dairy fats, meat fat) with mono- and polyunsaturated fatty acids (especially n-3 polyunsaturated fatty acids) (e.g.,

macadamia nuts, almonds, peanuts and peanut butter, olive oil, canola oil, avocados); avoidance of excessive intake of saturated fatty acids and cholesterol; pay attention to sucrose and fructose intake; increase intake of dietary fiber; and maintenance of good hydration. It is necessary to recognize how much micronutrient (vitamin and mineral) intake and alcohol consumption is important as potential dietary habits to prevent gout in Japanese people.

In this article, the author suggests the importance of micronutrient (vitamin and mineral) intake and alcohol consumption for prevention of gout in Japanese people referencing the results of clinical research reported.

## 2. Methods

### 2.1. The Number of Gout Patients

The number of gout patients was estimated in the Comprehensive Survey of Living Conditions performed by the Ministry of Health, Labour and Welfare in Japan

(1986-2016) [3]. The Comprehensive Survey of Living Conditions was based on self-reporting by residents. This article showed the rate of hospital visits due to gout from 1986 to 2016 based on the Comprehensive Survey of Living Conditions.

## 2.2. The Trends in Nutrient or Food Intake in Japanese People

The intake of nutrients or foods was searched in the National Health and Nutrition Survey Japan (1946-2017) performed by the Ministry of Health, Labour and Welfare in Japan [4-6].

Data were extracted from the series of Japanese National Nutrition Surveys that have been carried out every year throughout Japan since 1946 [6]. In these surveys, food consumption by families enrolled in the study was assessed by weighing food items consumed on three consecutive weekdays (until 1994) or one weekday (from 1995).

The daily nutrient or food intakes of Japanese people are shown as the mean values reported by the National Health and Nutrition Survey Japan (1946-2017) [4].

## 2.3. Dietary Reference Intakes for Japanese People

The Ministry of Health, Labour and Welfare in Japan [5] evaluated the intake of nutrients as described below: (1) the estimated average requirement (EAR) indicates the amount that would meet the nutrient requirements of 50% of the population; (2) the recommended dietary allowance (RDA) indicates the amount that would meet the nutrient requirement of most of the population; (3) the adequate intake (AI) indicates the amount adequate to maintain a certain level of nutritional status; (4) the tolerable upper intake level (UL) was determined for the purpose of avoiding adverse health effects due to excessive intake; and (5) the tentative dietary goal for preventing lifestyle-related diseases (DG) was developed for the purpose of prevention of lifestyle-related diseases.

## 2.4. Food Composition

The food composition was extracted from a standard tables of food composition in Japan -2020- (Eighth Revised Edition) of the Council for Science and Technology, Ministry of Education, Culture, Sports, Science and Technology in Japan. the Ministry of Education, Culture, Sports, Science and Technology [7] and the National Institutes of Health in the U.S. Department of Health & Human Services [8].

## 2.5. Statistical Analysis

The correlation efficient and the significance of the correlation between the number of gout patients and nutrient intake in 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, and 2016 were analyzed by Pearson Product Moment Correlation. A SigmaPlot 12.0 software program (version 12.0, Systat Software Inc, San Jose, CA) was used for statistical analysis. Differences were considered significant at  $p < 0.05$ .

## 3. Relationship Between the Number of Gout Patients and Vitamin Intake in Japanese People

The results on the correlation between the number of gout patients and vitamin intake in Japanese people are shown in Tables 1 and 2.

### 3.1. Fat-soluble Vitamins

#### 3.1.1. Vitamin A

The daily vitamin A (retinol equivalent) intake of Japanese people in 2016 was markedly higher compared to that in 1960, 1965, 1975, and 2013 and was lower compared to that in 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, and 2010 (1960: 354  $\mu\text{gRAE}$ ; 1965: 397.2  $\mu\text{gRAE}$ ; 1975: 480.6  $\mu\text{gRAE}$ ; 1986: 650.7  $\mu\text{gRAE}$ ; 1989: 806.1  $\mu\text{gRAE}$ ; 1992: 794.7  $\mu\text{gRAE}$ ; 1995: 852.0  $\mu\text{gRAE}$ ; 1998: 810.3  $\mu\text{gRAE}$ ; 2001: 981.0  $\mu\text{gRAE}$ ; 2004: 879.0  $\mu\text{gRAE}$ ; 2007: 615.0  $\mu\text{gRAE}$ ; 2010: 529.0  $\mu\text{gRAE}$ ; 2013: 516.0  $\mu\text{gRAE}$ ; 2016: 524.0  $\mu\text{gRAE}$ ). In Japanese men and women in 2016, the daily vitamin A (retinol equivalent) intake for men (aged 15-69 years), women (aged 15-19 years), and women (aged 30-49 years) was 465-574  $\mu\text{gRAE/day}$ , 450  $\mu\text{gRAE/day}$ , and 465-484  $\mu\text{gRAE/day}$ , respectively. In Japanese men and women in 2016, the daily vitamin A (retinol equivalent) intake for men (aged 15-69 years), women (aged 15-19 years), and women (aged 30-49 years) was below the estimated average requirement (EAR) [men (aged 15-69 years): 600-650  $\mu\text{gRAE/day}$ ; women (aged 15-19 years): 450-500  $\mu\text{gRAE/day}$ ; women (aged 30-49 years): 500  $\mu\text{gRAE/day}$ ] and the recommended dietary allowance (RDA) [men (aged 15-69 years): 850-900  $\mu\text{gRAE/day}$ ; women (aged 15-19 years): 650  $\mu\text{gRAE/day}$ ; women (aged 30-49 years): 700  $\mu\text{gRAE/day}$ ] [5]. In Japanese men and women in 2016, the daily vitamin A (retinol equivalent) intake for men (aged 1-14 years), men (aged  $\geq 70$  years), women (aged 1-14 years), women (aged 20-29 years), and women (aged  $\geq 50$  years) was 397-601  $\mu\text{gRAE/day}$ , 568  $\mu\text{gRAE/day}$ , 391-519  $\mu\text{gRAE/day}$ , 459  $\mu\text{gRAE/day}$ , and 520-569  $\mu\text{gRAE/day}$ , respectively. In Japanese men and women in 2016, the daily vitamin A (retinol equivalent) intake for men (aged 1-14 years), men (aged  $\geq 70$  years), women (aged 1-14 years), women (aged 20-29 years), and women (aged  $\geq 50$  years) was above the estimated average requirement (EAR) [men (1-14 years): 300-550  $\mu\text{gRAE/day}$ ; men (aged  $\geq 70$  years): 550-600  $\mu\text{gRAE/day}$ ; women (aged 1-14 years): 250-500  $\mu\text{gRAE/day}$ ; women (aged 20-29 years): 450  $\mu\text{gRAE/day}$ ; women (aged  $\geq 50$  years): 450-500  $\mu\text{gRAE/day}$ ] and was below the recommended dietary allowance (RDA) [men (aged 1-14 years): 400-800  $\mu\text{gRAE/day}$ ; men (aged  $\geq 70$  years): 800-850  $\mu\text{gRAE/day}$ ; women (aged 1-14 years): 350-700  $\mu\text{gRAE/day}$ ; women (aged 20-29 years): 650  $\mu\text{gRAE/day}$ ; women (aged  $\geq 50$  years): 650-700  $\mu\text{gRAE/day}$ ] [5]. The daily vitamin A (retinol equivalent) intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was below the recommended dietary allowance (RDA).

The daily vitamin A intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.899$ ,  $p = 0.000164$ ). The intake of vitamin A did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.669$ ,  $p = 0.217$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.731$ ,  $p = 0.161$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.797$ ,  $p = 0.106$ ). This result suggests that the daily vitamin A intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

Judging from the data of food composition [7, 8], it is important for Japanese people (aged  $\geq 1$  year) to eat organ meats (liver, breast), seafood (salmon, tuna, herring, firefly squid, eel, conger eel, sablefish), potatoes, whole grains (fortified ready-to-eat cereals), nuts (pistachio nuts), legumes (black-eyed peas, baked beans), seaweed, fruit (apricots, mangos, cantaloupes), vegetables (spinach, carrots, peppers, broccoli, Jew's mallows, perillas), dairy products (milk, cheese, yogurt), eggs, green tea to take in more vitamin A to reach the recommended dietary allowance (RDA).

### 3.1.2. Vitamin D

The daily vitamin D of Japanese people in 2016 was lower compared to that in 2001, 2004, and 2007 and was higher compared to that in 2010 and was about the same as that in 2013 (2001: 8.4  $\mu\text{g/day}$ ; 2004: 7.9  $\mu\text{g/day}$ ; 2007: 7.6  $\mu\text{g/day}$ ; 2010: 7.3  $\mu\text{g/day}$ ; 2013: 7.5  $\mu\text{g/day}$ ; 2016: 7.5  $\mu\text{g/day}$ ). In Japanese men and women in 2016, the daily vitamin D intake for men ( $\geq 1$  year) and women (aged  $\geq 1$  year) was 3.9-9.9  $\mu\text{g/day}$  and 3.6-8.9  $\mu\text{g/day}$ , respectively, and was below the tolerable upper intake level (UL) [men (aged  $\geq 1$  year): 20-100  $\mu\text{g/day}$ ; women (aged  $\geq 1$  year): 20-100  $\mu\text{g/day}$ ] [5]. In Japanese men and women in 2016, the daily vitamin D intake for men (aged 15-59 years) and women (aged 15-59 years) was 6.2-7.3  $\mu\text{g/day}$  and 5.7-7.2  $\mu\text{g/day}$ , respectively, and was below the adequate intake (AI) [men (aged 15-59 years): 8.5-9.0  $\mu\text{g/day}$ ; women (aged 15-59 years): 8.5  $\mu\text{g/day}$ ] [5]. In Japanese men and women in 2016, the daily vitamin D intake for men (aged  $\geq 60$  years) and women (aged  $\geq 60$  years) was 9.3-9.9  $\mu\text{g/day}$  and 8.6-8.9  $\mu\text{g/day}$ , respectively, and was above the adequate intake (AI) [men (aged  $\geq 60$  years): 8.5  $\mu\text{g/day}$ ; women (aged  $\geq 60$  years): 8.5  $\mu\text{g/day}$ ] [5]. The daily vitamin D intake of adult men and women tended to increase as age increased.

The daily vitamin D intake tended to be negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.809$ ,  $p = 0.0511$ ). The intake of vitamin D did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.723$ ,  $p = 0.167$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.870$ ,  $p = 0.0552$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.822$ ,  $p = 0.0876$ ). This result suggests that the correlation of daily vitamin D intake with the number of gout patients tends to vary with gender.

Judging from the data of food composition [7, 8] and roles in the body of vitamin D (promotion of calcium absorption, reduction of inflammation, modulation of such processes as cell growth, neuromuscular and immune function, and glucose metabolism) [8], it is important for Japanese people (aged  $\geq 1$  year) to eat fish (salmon, trout, swordfish, sturgeon, cisco, whitefish, mackerel, tuna, sardines, rockfish, tilapia, flatfish), fish oil (cod liver), mushrooms, milks (whole milk, whole chocolate milk, soy milk, almond milk), dairy products (yogurt), cereals (fortified ready-to-eat cereals), eggs to take in more vitamin D to reach the adequate intake (AI) or the recommended dietary allowances (RDAs) set by the National Institutes of Health [men (aged 1-70 years): 15  $\mu\text{g/day}$ ; men (aged  $> 70$  years): 20  $\mu\text{g/day}$ ; women (aged 1-70 years): 15  $\mu\text{g/day}$ ; women (aged  $> 70$  years): 20  $\mu\text{g/day}$ ] [8]. However, it must be careful not to exceed the tolerable upper intake level (UL) of the daily vitamin D intake.

### 3.1.3. Vitamin E

The daily vitamin E intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2010 and was about the same as that in 2013 (2001: 8.5 mg/day; 2004: 10.5 mg/day; 2007: 8.6 mg/day; 2010: 7.9 mg/day; 2013: 6.4 mg/day; 2016: 6.4 mg/day). In Japanese men and women in 2016, the daily vitamin E intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was 4.4-7.3 mg/day and 4.1-6.9 mg/day, respectively, and was below the tolerable upper intake level (UL) [men (aged  $\geq 1$  year): 150-900 mg/day; women (aged  $\geq 1$  year): 150-700 mg/day] [5]. In Japanese men and women in 2016, the daily vitamin E intake for men (aged 20-49 years) and women (aged  $\geq 20$  years) was 6.4-6.6 mg/day and 5.7-6.9 mg/day, respectively, and was above the adequate intake (AI) [men (aged 20-49 years): 6.0 mg/day; women (aged  $\geq 20$  years): 5.0-6.5 mg/day] [5]. This result suggests that the daily vitamin E intake in Japanese men (aged 20-49 years) and women (aged  $\geq 20$  years) appears to be very unlikely to cause a deficiency. The daily vitamin E intake for men (aged 50-59 years) in 2016 was 6.7 mg/day and was below the adequate intake (AI) [men (aged 50-59 years): 7.0 mg/day] [5].

The daily vitamin E intake did not show a significant correlation with the number of gout patients in 2001-2016 ( $r = -0.686$ ,  $p = 0.132$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.860$ ,  $p = 0.0613$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.671$ ,  $p = 0.215$ ). Whereas the daily vitamin E intake was negatively correlated with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.887$ ,  $p = 0.0446$ ).

Judging from the data of food composition [7, 8], it is important for Japanese men (aged 50-59 years) to eat wheat germ, seeds and nuts (sunflower seeds, almonds, hazelnuts, peanuts), vegetables (spinach, broccoli, tomatoes), and fruit (kiwi fruits, mangos) to take in more vitamin E to reach the adequate intake (AI).

### 3.1.4. Vitamin K

The daily vitamin K intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2010 and was

higher compared to that in 2013 (2001: 267 µg/day; 2004: 242 µg/day; 2007: 235 µg/day; 2010: 227 µg/day; 2013: 220 µg/day; 2016: 225 µg/day). In Japanese men and women in 2016, the daily vitamin K intake for men (aged ≥ 1 year) and women (aged ≥ 1 year) was 125-270 µg/day and 130-259 µg/day, respectively, and was above the adequate intake (AI) [men (aged ≥ 1 year): 60-160 µg/day; women (aged ≥ 1 year): 60-170 µg/day] [5]. This result suggests that the daily vitamin K intake in Japanese men (aged ≥ 1 year) and women (aged ≥ 1 year) appears to be very unlikely to cause a deficiency.

The daily vitamin K intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.923$ ,  $p = 0.00876$ ). The daily vitamin K intake tended to be negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2016 ( $r = -0.861$ ,  $p = 0.0608$ ). The daily vitamin K intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2016 ( $r = -0.826$ ,  $p = 0.0849$ ), and with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2016 ( $r = 0.630$ ,  $p = 0.255$ ).

Conscious intake of vitamin K-rich foods (e.g., natto, collards, turnip greens, spinach, kales, broccoli, soybeans, edamame, pumpkins, okra, pine nuts, blueberries, iceberg lettuces, chicken breast, grapes, cashews, carrots, chicken liver, ground beef) [7, 8] seems to be important.

## 3.2. Water-soluble Vitamins

### 3.2.1. Vitamin B<sub>1</sub>

The daily vitamin B<sub>1</sub> intake of Japanese people in 2016 was lower compared to that in 1960, 1965, 1975, 1986, 1989, 1992, 1995, 1998, 2001, and 2007 and was the same as that in 2004 and was higher compared to that in 2010 and 2013 (1960: 1.05 mg/day; 1965: 0.97 mg/day; 1975: 1.11 mg/day; 1986: 1.35 mg/day; 1989: 1.23 mg/day; 1992: 1.25 mg/day; 1995: 1.22 mg/day; 1998: 1.16 mg/day; 2001: 0.89 mg/day; 2004: 0.86 mg/day; 2007: 0.87 mg/day; 2010: 0.83 mg/day; 2013: 0.80 mg/day; 2016: 0.86 mg/day). In Japanese men and women in 2016, the daily vitamin B<sub>1</sub> intake for men (aged ≥ 1 year) and women (aged ≥ 1 year) was 0.58-1.12 mg/day and 0.56-0.85 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged ≥ 1 year): 0.5-1.5 mg/day; women (aged ≥ 1 year): 0.5-1.2 mg/day] [5].

The daily vitamin B<sub>1</sub> intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.949$ ,  $p = 0.00000799$ ), and with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2016 ( $r = -0.909$ ,  $p = 0.0327$ ). The daily vitamin B<sub>1</sub> intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2016 ( $r = -0.860$ ,  $p = 0.0614$ ), and with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2016 ( $r = 0.263$ ,  $p = 0.669$ ). This result suggests that the daily vitamin B<sub>1</sub> intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

In an epidemiological study, increased vitamin B<sub>1</sub> intake was associated with decreased serum uric acid (SUA) concentrations [9]. It is possible that vitamin B<sub>1</sub> intake prevent

gout through a decrease in SUA concentrations.

Judging from the data of food composition [7, 8], it is important for Japanese people (aged ≥ 1 year) to eat meats (pork), seafood (mussels, trout, tuna, walleye pollock, eel), mushrooms (maitake mushrooms), grains (white rice, egg noodle, bread), whole grains (whole wheat, brown rice, oatmeal, fortified ready-to-eat cereals), seeds (sunflower seeds, sesame seeds, chia seeds), legumes (black beans, soybeans), fruit (avocados), vegetables (broccoli), dairy products (milk), eggs to take in more vitamin B<sub>1</sub> to reach the recommended dietary allowance (RDA).

### 3.2.2. Vitamin B<sub>2</sub>

The daily vitamin B<sub>2</sub> intake of Japanese people in 2016 was higher compared to that in 1960, 1965, 1975, 2010, and 2013 and was lower compared to that in 1986, 1989, 1992, 1995, 1998, 2001, 2004, and 2007 (1960: 0.72 mg/day; 1965: 0.83 mg/day; 1975: 0.96 mg/day; 1986: 1.26 mg/day; 1989: 1.33 mg/day; 1992: 1.36 mg/day; 1995: 1.47 mg/day; 1998: 1.42 mg/day; 2001: 1.22 mg/day; 2004: 1.17 mg/day; 2007: 1.17 mg/day; 2010: 1.13 mg/day; 2013: 1.10 mg/day; 2016: 1.15 mg/day). In Japanese men and women in 2016, the daily vitamin B<sub>2</sub> intake for men (aged ≥ 10 years) and women (aged ≥ 10 years) was 1.10-1.32 mg/day and 1.01-1.20 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged ≥ 10 years): 1.30-1.70 mg/day; women (aged ≥ 10 years): 1.0-1.4 mg/day] [5].

The daily vitamin B<sub>2</sub> intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.799$ ,  $p = 0.00468$ ), with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2016 ( $r = -0.923$ ,  $p = 0.0256$ ), and with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2016 ( $r = -0.941$ ,  $p = 0.0170$ ). The daily vitamin B<sub>2</sub> intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2016 ( $r = 0.289$ ,  $p = 0.638$ ). This result suggests that the correlation of daily vitamin B<sub>2</sub> intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women. This result suggests that the daily vitamin B<sub>2</sub> intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

In an epidemiological study, increased vitamin B<sub>2</sub> intake was associated with decreased serum uric acid (SUA) concentrations [9]. It is possible that vitamin B<sub>2</sub> intake prevent gout through a reduction of SUA concentrations.

Judging from the data of food composition [7, 8], it is important for Japanese men (aged ≥ 10 years) and women (aged ≥ 10 years) to eat organ meats (kidneys, liver), seafood (clams, salmon, cod), mushrooms (maitake mushrooms, shiitake mushrooms), grains (white rice, egg noodle, bread), whole grains (whole wheat, brown rice, oats, fortified ready-to-eat cereals), seeds (sunflower seeds, almonds), legumes (kidney beans), seaweed, vegetables (asparagus, tomatoes, cauliflowers), dairy products (milk, cheese, yogurt), eggs to take in more vitamin B<sub>2</sub> to reach the recommended dietary allowance (RDA).

### 3.2.3. Niacin (Vitamin B<sub>3</sub>)

The daily niacin intake of Japanese people in 2016 was lower compared to that in 2001, 2004, and 2007 and was higher compared to that in 2010 and was the same as that in 2013 (2001: 15.1 mg NE /day; 2004: 14.9 mg NE /day; 2007: 15.0 mg NE /day; 2010: 14.2 mg NE /day; 2013: 14.4 mg NE /day; 2016: 14.4 mg NE /day). In Japanese men and women in 2016, the daily niacin intake for men (aged  $\geq 7$  years) and women (aged  $\geq 7$  years) was 13.1-17.8 mg NE /day and 11.2-15.1 mg NE /day, respectively, and was above the recommended dietary allowance (RDA) [men (aged  $\geq 7$  years): 9.0-17.0 mg NE /day; women (aged  $\geq 7$  years): 8.0-14.0 mg NE /day] [5]. The daily niacin intake for men (aged  $\geq 7$  years) and women (aged  $\geq 7$  years) was below the tolerable upper intake level (UL) [men (aged  $\geq 7$  years): 100-350 mg NE /day; women (aged  $\geq 7$  years): 100-250 mg NE /day] [5]. It seems that the daily niacin intake of Japanese people in 2016 was appropriate.

The daily niacin intake did not show a significant correlation with the number of gout patients in 2001-2016 ( $r=0.113$ ,  $p=0.831$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.755$ ,  $p=0.140$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r=0.786$ ,  $p=0.115$ ). The daily niacin intake was negatively correlated with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.884$ ,  $p=0.0467$ ). This result suggests that the correlation of daily niacin intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

### 3.2.4. Pantothenic Acid (Vitamin B<sub>5</sub>)

The daily pantothenic acid intake of Japanese people in 2016 was lower compared to that in 2001, 2004, and 2007 and was higher compared to that in 2010 and 2013 (2001: 5.71 mg/day; 2004: 5.52 mg/day; 2007: 5.46 mg/day; 2010: 5.24 mg/day; 2013: 5.41 mg/day; 2016: 5.45 mg/day). In Japanese men and women in 2016, the daily pantothenic acid intake for men (aged 18-49 years and 60-69 years), and women (aged  $\geq 50$  years) was 6.47-5.58 mg/day, 6.09 mg/day, and 5.18-5.53 mg/day, respectively, and was above the adequate intake (AI) [men (aged 18-49 years): 5.0 mg/day; men (aged 60-69 years): 6.0 mg/day; women (aged  $\geq 50$  years): 5.0 mg/day] [5]. In Japanese men and women in 2016, the daily pantothenic acid intake for men (aged 1-17 years, aged 50-59 years, aged  $\geq 70$  years) and women (aged 1-49 years) was 3.96-6.47 mg/day, 5.85 mg/day, 5.95 mg/day, and 3.84-4.78 mg/day, respectively, and was below the adequate intake (AI) [men (aged 1-17 years): 3.0-7.0 mg/day; men (aged 50-59 years): 6.0 mg/day; men (aged  $\geq 70$  years): 6.0 mg/day; women (aged 1-49 years): 4.0-6.0 mg/day] [5].

The daily pantothenic acid intake did not show a significant correlation with the number of gout patients in 2001-2016 ( $r=-0.663$ ,  $p=0.151$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.027$ ,  $p=0.966$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.0376$ ,  $p=0.952$ ), and with the

number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r=0.651$ ,  $p=0.234$ ).

The daily pantothenic acid intake in Japanese men (aged 18-49 years and 60-69 years) and women (aged  $\geq 50$  years) appears to be very unlikely to cause a deficiency. Judging from the data of food composition [7, 8], it is important for Japanese men (aged 1-17 years, aged 50-59 years, aged  $\geq 70$  years) and women (aged 1-49 years) to eat meats (beef, poultry), seafood, organ meats, mushrooms (shiitake mushrooms), potatoes, whole grains (whole wheat, brown rice, oats), nuts (peanuts), seeds (sunflower seeds), legumes (chickpeas), fruit (avocados), vegetables (broccoli), dairy products (milk), eggs to take in more pantothenic acid.

### 3.2.5. Vitamin B<sub>6</sub>

The daily vitamin B<sub>6</sub> intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2010 and was the same as that in 2013 (2001: 1.18 mg/day; 2004: 1.72 mg/day; 2007: 1.67 mg/day; 2010: 1.67 mg/day; 2013: 1.11 mg/day; 2016: 1.11 mg/day). In Japanese men and women in 2016, the daily vitamin B<sub>6</sub> intake for men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) was 1.11-1.32 mg/day and 0.95-1.18 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged  $\geq 15$  years): 1.40-1.50 mg/day; women (aged  $\geq 15$  years): 1.1-1.3 mg/day] [5].

The daily vitamin B<sub>6</sub> intake was negatively correlated with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.931$ ,  $p=0.0213$ ), and with number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r=-0.927$ ,  $p=0.0232$ ). The daily vitamin B<sub>6</sub> intake did not show a significant correlation with the number of gout patients in 2001-2016 ( $r=-0.300$ ,  $p=0.563$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r=0.266$ ,  $p=0.666$ ). This result suggests that the correlation of daily vitamin B<sub>6</sub> intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women. This result suggests that the daily vitamin B<sub>6</sub> intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

Judging from the data of food composition [7, 8], it is important for Japanese men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) to eat meats (turkey, chicken, pork fin), organ meats (chicken breast, beef liver, pork liver), seafood (tuna, salmon, skipjack, sardines, mackerel, Nile tilapia), grains (white rice, buckwheat), whole grains (fortified ready-to-eat cereals), potatoes, seeds and nuts (sunflower seeds, squid, pistachio nuts, sesame seeds), legumes (chickpeas), seaweed, vegetables (onions, garlic, tomatoes, peppers), fruit (bananas, raisins, watermelons), dairy products (cheese), soy products (tofu) to take in more vitamin B<sub>6</sub> to reach the recommended dietary allowance (RDA).

### 3.2.6. Folate (Vitamin B<sub>9</sub>)

The daily folate intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, 2010, and 2013 (2001: 313.0  $\mu\text{g/day}$ ; 2004: 294.0  $\mu\text{g/day}$ ; 2007: 299.0  $\mu\text{g/day}$ ; 2010: 281.0  $\mu\text{g/day}$ ; 2013: 280.0  $\mu\text{g/day}$ ; 2016: 277.0  $\mu\text{g/day}$ ).

In Japanese men and women in 2016, the daily folate intake for men (aged 1-6 years, aged  $\geq 15$  years) and women (aged 1-6 years, aged  $\geq 40$  years) was 156  $\mu\text{g/day}$ , 244-334  $\mu\text{g/day}$ , 151  $\mu\text{g/day}$ , and 244-318  $\mu\text{g/day}$ , respectively, and was above the recommended dietary allowance (RDA) [men (aged 1-6 years): 90.0-140.0  $\mu\text{g/day}$ ; men (aged  $\geq 15$  years): 240.0  $\mu\text{g/day}$ ; women (aged 1-6 years): 90.0-140.0  $\mu\text{g/day}$ ; women (aged  $\geq 40$  years): 240.0  $\mu\text{g/day}$ ] and was below the tolerable upper intake level (UL) [men (aged 1-6 years): 20.0-400.0  $\mu\text{g/day}$ ; men (aged  $\geq 15$  years): 900.0-1000.0  $\mu\text{g/day}$ ; women (aged 1-6 years): 200.0-400.0  $\mu\text{g/day}$ ; women (aged  $\geq 40$  years): 900.0-1000.0  $\mu\text{g/day}$ ] [5]. In Japanese men and women in 2016, the daily folate intake for men (aged 7-14 years) and women (aged 7-29 years) was 236.0  $\mu\text{g/day}$  and 218-229  $\mu\text{g/day}$ , respectively, and was below the recommended dietary allowance (RDA) [men (aged 7-14 years): 140.0-240.0  $\mu\text{g/day}$ ; women (aged 7-29 years): 140.0-240.0  $\mu\text{g/day}$ ] [5]. In Japanese men and women in 2016, the daily folate intake for women (aged 30-39 years) was 240.0  $\mu\text{g/day}$  and was the same as that for the recommended dietary allowance (RDA) [women (aged 30-39 years): 240.0  $\mu\text{g/day}$ ] [5]. The daily folate intake of adult men and women tended to increase as age increased.

The daily folate intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.967$ ,  $p = 0.00165$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.947$ ,  $p = 0.0144$ ), and with the number of gout patients in the adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.922$ ,  $p = 0.0258$ ). The daily folate intake did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.690$ ,  $p = 0.198$ ). This result suggests that the correlation of daily folate intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

In epidemiological studies, increased folate intake was associated with decreased serum uric acid (SUA) concentrations [9] and gout risk [10]. It is possible that folate intake prevent gout through a decrease in SUA concentrations.

Judging from the data of food composition [7, 8], it is important for Japanese men (aged 7-14 years) and women (aged 7-29 years) to eat meats (beef), organ meats (liver, breast), seafood (crab, halibut, sardines, sea urchin), mushrooms (maitake mushrooms, shiitake mushrooms), grains (white rice, spaghetti, bread, wheat), whole grains (fortified ready-to-eat cereals), seeds (sunflower seeds, peanuts), legumes (black-eyed peas, kidney beans, green peas, soybeans, chickpeas), seaweed, fruit (avocados, oranges, papayas, bananas, mangos), vegetables (asparagus, spinach, brussels sprouts, lettuces, broccoli, mustard greens, Jew's mallow), dairy products (milk), eggs, green tea to take in more folate to reach the recommended dietary allowance (RDA).

### 3.2.7. Vitamin B<sub>12</sub>

The daily vitamin B<sub>12</sub> intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2013 and

was the same as that in 2010 (2001: 7.7  $\mu\text{g/day}$ ; 2004: 7.0  $\mu\text{g/day}$ ; 2007: 7.1  $\mu\text{g/day}$ ; 2010: 6.0  $\mu\text{g/day}$ ; 2013: 6.1  $\mu\text{g/day}$ ; 2016: 6.0  $\mu\text{g/day}$ ). In Japanese men and women in 2016, the daily vitamin B<sub>12</sub> intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was 3.5-7.8  $\mu\text{g/day}$  and 2.9-6.7  $\mu\text{g/day}$ , respectively, and was above the recommended dietary allowance (RDA) [men (aged  $\geq 1$  year): 0.9-2.4  $\mu\text{g/day}$ ; women (aged  $\geq 1$  year): 0.9-2.4  $\mu\text{g/day}$ ] [5]. The daily vitamin B<sub>12</sub> intake of adult men and women tended to increase as age increased. The Ministry of Health, Labour and Welfare in Japan [5] has not set a tolerable upper intake level (UL) for healthy people because there is no scientific evidence for health problems due to excessive daily intake of vitamin B<sub>12</sub>.

The daily vitamin B<sub>12</sub> intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.936$ ,  $p = 0.00599$ ). The vitamin B<sub>12</sub> intake tended to be negatively correlated with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.851$ ,  $p = 0.0677$ ). The daily vitamin B<sub>12</sub> intake was negatively correlated with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.923$ ,  $p = 0.0255$ ). Whereas the daily vitamin B<sub>12</sub> intake was positively correlated with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.880$ ,  $p = 0.0492$ ). This result suggests that the correlation of daily vitamin B<sub>12</sub> intake with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The Ministry of Health, Labour and Welfare in Japan [5] has stated that the recommended daily vitamin B<sub>12</sub> intake in men and women (aged  $\geq 1$  year) of 0.9-2.4  $\mu\text{g/day}$  may be low and has been considered a future issue to address. The daily vitamin B<sub>12</sub> intake seems to be appropriate or it seems better to increase it slightly.

### 3.2.8. Vitamin C

The vitamin C intake of Japanese people in 2016 was higher compared to that in 1960 and 1965 and was lower compared to that in 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, and 2013 (1960: 75.0 mg/day; 1965: 78.0 mg/day; 1975: 117.0 mg/day; 1986: 124.0 mg/day; 1989: 123.0 mg/day; 1992: 122.0 mg/day; 1995: 135.0 mg/day; 1998: 125.0 mg/day; 2001: 106.0 mg/day; 2004: 99.0 mg/day; 2007: 96.0 mg/day; 2010: 90.0 mg/day; 2013: 94.0 mg/day; 2016: 89.0 mg/day). In Japanese men and women in 2016, the daily vitamin C intake for men (aged 10-59 years) and women (aged 8-59 years) was 65.0-82.0 mg/day and 66.0-90.0 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged 10-59 years): 85.0-100.0 mg/day; women (aged 8-59 years): 70.0-100.0 mg/day] [5]. In Japanese men and women in 2016, the daily vitamin C intake for men (aged  $\geq 60$  years) and women (aged  $\geq 60$  years) was 105.0-119.0 mg/day and 115-121 mg/day, respectively, and exceeded the recommended dietary allowance (RDA) [men (aged  $\geq 60$  years): 100.0 mg/day; women (aged  $\geq 60$  years): 100.0 mg/day] [5]. The Ministry of Health, Labour and Welfare in Japan [5] has not set a tolerable upper intake level (UL) for

healthy people because there is no scientific evidence for health problems due to excessive daily vitamin C intake.

The daily vitamin C intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.914$ ,  $p = 0.0000845$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.979$ ,  $p = 0.00360$ ), and with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.948$ ,  $p = 0.0142$ ). The daily intake of vitamin C did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.552$ ,  $p = 0.335$ ). This result suggests that the correlation of daily vitamin C intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women. This result suggests that the daily vitamin C intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

In clinical trials, vitamin C decreased serum uric acid (SUA) concentrations [11-15]. In epidemiological studies, increased intake of vitamin C was associated with decreased SUA concentrations [16-19], hyperuricemia risk [16, 18, 20], and gout risk [10, 21-23]. Vitamin C intake may prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

Vitamin C lowers SUA concentration through a uricosuric effect by competing with SUA on the urate transporter 1 (also known as solute carrier family 22, member 12, or SLC22A12) for re-absorption in the kidney proximal tubule [11, 13-15, 24]. Vitamin C inhibits the pro-oxidant actions of UA during copper-mediated low density lipoprotein cholesterol (LDL-cholesterol) oxidation, and could reduce oxidative stress and inflammation, and may be related to lower UA production [25].

The British Society for Rheumatology Guidelines (ACR) for the Management of Gout [26] and the 2020 American College of Rheumatology guideline for the management of gout [27] have recommended vitamin C intake for patients with gout. However, a randomized trial of vitamin C 500 mg daily as an adjunct to allopurinol demonstrated no reduction in SUA levels with vitamin C [28].

Judging from the data of food composition [7, 8], it is important for Japanese men (aged 10-59 years) and women (aged 8-59 years) to eat seaweed, fruit (acerolas, guavas, kiwi fruits, lemons, strawberries, papayas, blackcurrants), vegetables (kales, peppers, parsley, broccoli, tomatoes, cauliflowers, peas, eggplants, brussels sprouts, Chinese cabbages, mustard spinach) to take in more vitamin C to reach the recommended dietary allowance (RDA).

## 4. Relationship Between the Number of Gout Patients and Mineral Intake in Japanese People

The results on the correlation between the number of gout patients and intake of mineral or salt in Japanese people are shown in Tables 1 and 2.

**Table 1.** Correlation between number of gout patients and intake of micronutrient or salt in Japanese people in 1986-2016.

Micronutrient	coefficient	p-value
Vitamins		
Vitamin A*	- 0.899	0.000164
Vitamin B <sub>1</sub> *	- 0.949	0.00000799
Vitamin B <sub>2</sub> *	- 0.799	0.00468
Vitamin C	- 0.914	0.0000845
Minerals		
Calcium*	- 0.714	0.0136
Iron	- 0.909	0.000107
Salt**	- 0.903	0.000141

\*The daily micronutrient intake of Japanese people (aged  $\geq 15$  years) in 2016 was below the recommended dietary allowance (RDA). \*\*The daily salt intake of Japanese people (aged  $\geq 1$  year) in 2016 exceeded the tentative dietary goal for preventing lifestyle-related diseases (DG).

**Table 2.** Correlation between number of gout patients and micronutrient intake in Japanese people in 2001-2016.

Micronutrient	coefficient	p-value
Vitamins		
Vitamin D	- 0.809	0.0511
Vitamin E	- 0.686	0.132
Vitamin K	- 0.923	0.00876
Niacin	0.113	0.831
Pantothenic acid	- 0.663	0.151
Vitamin B <sub>6</sub> *	- 0.300	0.563
Folate	- 0.967	0.00165
Vitamin B <sub>12</sub> **	- 0.936	0.00599
Minerals		
Potassium*	- 0.905	0.0132
Magnesium*	- 0.904	0.0135
Phosphorus	- 0.858	0.0289
Copper	- 0.933	0.00652
Zinc*	- 0.868	0.0205

\*The daily micronutrient intake of Japanese people (aged  $\geq 15$  years) in 2016 was below the recommended dietary allowance (RDA). \*\*The daily vitamin B<sub>12</sub> intake of Japanese people (aged  $\geq 1$  year) in 2016 was above the recommended dietary allowance (RDA).

### 4.1 Macrominerals

#### 4.1.1. Sodium and Salt

##### 1. Sodium

The daily sodium intake of Japanese people in 2016 was lower compared to that in 1995, 1998, 2000, 2002, 2005, 2007, 2010, and 2013 (1995: 5.18 g/day; 1998: 5.00 g/day; 2000: 4.85 g/day; 2002: 4.48 g/day; 2005: 4.32 g/day; 2007: 4.18 g/day; 2010: 4.00 g/day; 2013: 3.87 g/day; 2016: 3.77 g/day). In Japanese men and women in 2016, the daily sodium intake for men (aged  $\geq 20$  years) and women (aged  $\geq 20$  years) was 3995-4494 mg/day and 3352-3842 mg/day, respectively, and exceeded the estimated average requirement (EAR) [men (aged  $\geq 20$  years): 600 mg/day; women (aged  $\geq 20$  years): 600 mg/day] [5]. Though the daily sodium intake was negatively correlated with the number of gout patients in 1995-2016 ( $r = -0.990$ ,  $p = 0.000160$ ), it seems that the daily sodium intake for Japanese men and women in 2016 is excessive.

Excess sodium intake among the population was associated with higher risk of major non-communicable diseases such as hypertension, cardiovascular disease (CVD) and stroke [29]. Although the National Health and Nutrition Survey in Japan

have reported decreasing sodium intake among Japanese population since 1974 to 2015 (14.5 to 9.7 g/day) [30], high sodium intake is still on the top of cardiovascular risk factors of Japanese population [31].

Japanese Society of Nephrology have recommended limiting sodium intake to 3-6 g/day in chronic kidney disease (CKD) patients [32]. Two guidelines have recommended limiting sodium intake to less than 100 mmol/L/day (or < 2.3 g/day) in adults with CKD (CKD stages 3-5, 5D) or posttransplantation [33] and in patients with diabetes [34].

## 2. Salt

The daily salt intake of Japanese people in 2016 was lower compared to that in 1975, 1980, 1985, 1986, 1995, 1998, 2001, 2004, 2007, 2010, and 2013 (1975: 13.5 g/day; 1980: 12.9 g/day; 1985: 12.1 g/day; 1986: 12.1 g/day; 1995: 13.2 g/day; 1998: 12.7 g/day; 2001: 11.5 g/day; 2004: 10.7 g/day; 2007: 10.6 g/day; 2010: 10.2 g/day; 2013: 9.8 g/day; 2016: 9.6 g/day). In Japanese men and women in 2016, the daily salt intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was 5.3-11.4 g/day and 5.4-9.8 g/day, respectively, and exceeded the tentative dietary goal for preventing lifestyle-related diseases (DG) [men (aged  $\geq 1$  year): < 3.0-7.5 g/day; women (aged  $\geq 1$  year): < 3.0-6.5 g/day] [5]. The daily salt intake of adult men and women tended to increase as age increased. It is speculated that a decrease in daily salt intake in the situation of exceeding the tentative dietary goal for preventing lifestyle-related diseases (DG) is associated with the number of patients with gout. Thus, it is important for Japanese people to reduce salt intake.

The daily salt intake was negatively correlated with number of gout patients in 1986-2016 ( $r = -0.903$ ,  $p = 0.000141$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.988$ ,  $p = 0.00164$ ), and with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.992$ ,  $p = 0.000801$ ). The daily salt intake did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.722$ ,  $p = 0.169$ ). This result suggests that the correlation of daily salt intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The guidelines recommended the following for salt intake: (1) limit intake of salt in gout patients [35]; (2) limit salt intake (4-5 g/day) for patients with urolithiasis [36]; (3) limit salt overdose ( $\leq 10$  g/day) for patients with urolithiasis [37]; (4) salt reduction for patients with hypertension [38]; (5) limit salt intake (< 6 g/day) for patients with hypertension [39]; (6) salt intake less than 7.5 g/day for men with diabetes mellitus and less than 6.5 g/day for women with diabetes mellitus [40]; and (7) reducing intake of salt (to less than 5 g or 90 mmol per day) is likely to be beneficial for the prevention of cardiovascular disease (CVD) in healthy adults [41, 42].

### 4.1.2. Calcium

The calcium intake of Japanese people in 2016 was higher compared to that in 1960 and 1965 and was lower compared to that in 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, and 2013 (1960: 389.0 mg/day; 1965: 465.0 mg/day;

1975: 550.0 mg/day; 1986: 551.0 mg/day; 1989: 540.0 mg/day; 1992: 539.0 mg/day; 1995: 585.0 mg/day; 1998: 568.0 mg/day; 2001: 550.0 mg/day; 2004: 538.0 mg/day; 2007: 531.0 mg/day; 2010: 510.0 mg/day; 2013: 504.0 mg/day; 2016: 502.0 mg/day). In Japanese men and women in 2016, the daily calcium intake for men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) was 430-562 mg/day and 396-543 mg/day, respectively, and was below the estimated average requirement (EAR) [men (aged  $\geq 15$  years): 600-650 mg/day; women (aged  $\geq 15$  years): 550 mg/day] and the recommended dietary allowance (RDA) [men (aged  $\geq 15$  years): 700-800 mg/day; women (aged  $\geq 15$  years): 600-650 mg/day] [5]. In Japanese men and women in 2016, the daily calcium intake for men (aged 1-14 years) and women (aged 1-14 years) was 421-678 mg/day and 398-610 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged 1-14 years): 450-1000 mg/day; women (aged 1-14 years): 400-800 mg/day] [5].

The daily calcium intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.714$ ,  $p = 0.0136$ ), and with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.952$ ,  $p = 0.0124$ ). The daily calcium intake did not show a significant correlation with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.848$ ,  $p = 0.0693$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.769$ ,  $p = 0.128$ ). This result suggests that the correlation of daily calcium intake with the number of gout patients tends to vary with gender and tended to be stronger in adult men than in adult women. This result suggests that the daily calcium intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

In epidemiological studies, increased intake of calcium was associated with decreased serum uric acid (SUA) concentrations [9, 43] and hyperuricemia risk [20]. It is possible that calcium intake prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

The guidelines recommended the following for calcium intake: (1) prescribe a total elemental calcium intake of 800-1,000 mg/day (including dietary calcium, calcium supplementation, and calcium-based phosphate binders) in adults with chronic kidney disease (CKD) (CKD stages 3-4) not taking active vitamin D analogs [33]; (2) normal calcium content (1-1.2 g/day) for patients with urolithiasis [36]; and (3) calcium intake (600-800 mg/day) for patients with urolithiasis [37].

Judging from the data of food composition [7, 8], it is important for Japanese people (aged  $\geq 1$  year) to eat seafood (sardines), cereals (fortified ready-to-eat cereals), milks (almond milk, low-fat milk, skim milk, whole butter milk, whole chocolate milk), vegetables (spinach, okra, curly kale), dairy products (milk, cheese, yogurt), soy products (soy milk, tofu) to take in more calcium to reach the recommended dietary allowance (RDA).

### 4.1.3. Potassium

The daily potassium intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2013 and was

higher compared to that in 2010 (2001: 2434 mg/day; 2004: 2321 mg/day; 2007: 2306 mg/day; 2010: 2200 mg/day; 2013: 2231 mg/day; 2016: 2219 mg/day). In Japanese men and women in 2016, the daily potassium intake for men (aged 15-59 years) and women (aged 15-49 years) was 1998-2291 mg/day and 1782-1937 mg/day, respectively, and was below the adequate intake (AI) [men (aged 15-59 years): 2500-2700 mg/day; women (aged 15-49 years): 2000 mg/day] [5]. Whereas the daily potassium intake for men (aged  $\geq 60$  years) and women (aged  $\geq 50$  years) was 2556-2603 mg/day and 2217-2476 mg/day, respectively, and was above the adequate intake (AI) [men (aged  $\geq 60$  years): 2500 mg/day; women (aged  $\geq 50$  years): 2000 mg/day] [5]. In Japanese men and women in 2016, the daily potassium intake for men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) was 1998-2603 mg/day and 1782-2476 mg/day, respectively, and was below tentative dietary goal for preventing life-style related diseases (DG) [men (aged  $\geq 15$  years):  $\geq 3000$  mg/day; women (aged  $\geq 15$  years):  $\geq 2600$  mg/day] [5]. The daily potassium intake of Japanese people tended to increase as age increased. This result suggests that the daily potassium intake below the recommended dietary allowance (RDA) is related to the increase in the number of gout patients.

The daily potassium intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.905$ ,  $p = 0.0132$ ). The daily potassium intake did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.773$ ,  $p = 0.126$ ), and with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.808$ ,  $p = 0.0977$ ). The daily potassium intake tended to be positively correlated with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.863$ ,  $p = 0.0594$ ). This result suggests that the correlation of daily potassium intake with number of gout patients tends to vary with gender.

Clinical practice guideline for nutrition in chronic kidney disease (CKD) have recommended controlling serum potassium concentrations (4.0 mEq/L ~ 5.5 mEq/L) in CKD [32] and adjusting potassium intake to maintain serum potassium levels within the normal range in adults with CKD (CKD stages 3-5D) or posttransplantation [33].

Judging from the data of food composition [7, 8], it is important for Japanese men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) to eat meats (poultry), seafood (tuna, halibut, cod, trout, rockfish), nuts, whole grains (brown and wild rice, brown cereal, whole-wheat bread and pasta), potatoes, legumes (peas, lima beans, pinto beans, kidney beans, soybeans, lentils), mushrooms, fruit (bananas, oranges, apricots, grapefruits, cantaloupes), vegetables (spinach, broccoli, cucumbers, zucchinis, pumpkins, leafy greens), coffee to take in more potassium to reach the tentative dietary goal for preventing lifestyle-related diseases (DG). It is encouraged to replace meat with fish and legumes.

#### 4.1.4. Magnesium

The daily magnesium intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2013 and

was higher compared to that in 2010 (2001: 262 mg/day; 2004: 250 mg/day; 2007: 247 mg/day; 2010: 236 mg/day; 2013: 239 mg/day; 2016: 238 mg/day). In Japanese men and women in 2016, the daily magnesium intake for men (aged 1-6 years), men (aged  $\geq 70$  years), women (aged 1-6 years), and women (aged  $\geq 60$  years) was 148 mg/day, 278 mg/day, 146 mg/day, and 247-259 mg/day, respectively, and was above the estimated average requirement (EAR) [men (aged 1-6 years): 60-110 mg/day; men (aged  $\geq 70$  years): 270 mg/day; women (aged 1-6 years): 60-110 mg/day; women (aged  $\geq 60$  years): 220-240 mg/day] [5]. In Japanese men and women in 2016, the daily magnesium intake for men (aged 1-6 years) and women (aged 1-6 years) was above the recommended dietary allowance (RDA) [men (aged 1-6 years): 70-130 mg/day; women (aged 1-6 years): 70-130 mg/day] [5]. In Japanese men and women in 2016, the daily magnesium intake for men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) was 222-284 mg/day and 189-259 mg/day, respectively, and was below the recommended dietary allowance (RDA) [men (aged  $\geq 15$  years): 320-370 mg/day; women (aged  $\geq 15$  years): 260-310 mg/day] [5]. In Japanese men and women in 2016, the daily magnesium intake for men (aged 7-14 years) and women (aged 7-14 years) was 232 mg/day and 209 mg/day, respectively. The Ministry of Health, Labour and Welfare in Japan [5] has set the tolerable upper intake level (UL) of daily magnesium intake for men and women (aged 7-14 years) and men and women (aged  $\geq 15$  years) was 5 mg/kg body weight/day and 350 mg/day, respectively. In healthy men and women (aged 1-14 years), overdose of magnesium-rich foods and/or supplementation should be avoided so as not to exceed the tolerable upper intake level (UL).

The daily magnesium intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.904$ ,  $p = 0.0135$ ). The daily magnesium intake did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.815$ ,  $p = 0.0925$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.839$ ,  $p = 0.0755$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.851$ ,  $p = 0.0672$ ). This result suggests that the correlation of daily magnesium intake with the number of gout patients tends to vary with gender.

In an epidemiological study, increased magnesium intake was associated with decreased serum uric acid (SUA) concentrations [44] and hyperuricemia risk [44]. It is possible that magnesium intake prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

Judging from the data of food composition [7, 8], it is important for Japanese men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) to eat meats (beef), organ meats (chicken breast), seafood (salmon, sardines), seeds and nuts (pumpkin seeds, chia seeds, sunflower seeds, almonds, peanuts, cashew nuts, sesame seeds, flaxseeds), grains (white rice, bread), whole grains (brown rice, cereals, fortified ready-to-eat cereals, whole-wheat bread, oatmeal), potatoes, legumes (black beans, kidney beans, edamame), seaweeds, fruit (bananas, raisins, avocados, apples), vegetables (spinach,

broccoli, carrots, parsley), dairy products (milk, yogurt), soy products (soy milk), tea, green tea to take in more magnesium to reach the recommended dietary allowance (RDA).

#### 4.1.5. Phosphorus

The daily phosphorus intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, and 2013 and was higher compared to that in 2010 (2001: 1057 mg/day; 2004: 1013 mg/day; 2007: 1000 mg/day; 2010: 960 mg/day; 2013: 978 mg/day; 2016: 976 mg/day). In Japanese men and women in 2016, the daily phosphorus intake for men (aged 20-39 years) was 983-988 mg/day and was below the adequate intake (AI) [men (aged 20-39 years): 1000 mg/day] [5]. Whereas the daily phosphorus intake for men (aged  $\geq 40$  years) and women (aged  $\geq 20$  years) was 1004-1119 mg/day and 827-996 mg/day, respectively, and was above the adequate intake (AI) [men (aged  $\geq 40$  years): 1000 mg/day; women (aged  $\geq 20$  years): 800 mg/day] and was below the tolerable upper intake level (UL) [men (aged  $\geq 40$  years): 3000 mg/day; women (aged  $\geq 20$  years): 3000 mg/day] [5].

The daily phosphorus intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.858$ ,  $p = 0.0289$ ). The daily phosphorus intake did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.594$ ,  $p = 0.291$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.649$ ,  $p = 0.236$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.845$ ,  $p = 0.0713$ ). This result suggests that the correlation of daily phosphorus intake with the number of gout patients tends to vary with gender.

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) [33] has recommended phosphorus restriction treatment to consider the bioavailability of phosphorus sources (e.g., animal, vegetable, additives) in adults with chronic kidney disease (CKD) (CKD stages 1-5D) or posttransplantation.

The daily phosphorus intake in Japanese men (aged  $\geq 40$  years) and women (aged  $\geq 20$  years) appears to be very unlikely to cause a deficiency. Judging from the data of food composition [7, 8], it is important for Japanese men (aged 20-39 years) to eat meats (chicken), seafood (salmon, scallops), potatoes, whole grains (whole wheat, brown rice, bran cereals, oatmeal), seeds (sesame seeds), nuts (cashew nuts), legumes (green peas, kidney beans), vegetables (asparaguses, tomatoes, cauliflowers), fruit (apples), dairy products (milk, cheese, yogurt), eggs to take in more phosphorus to reach the adequate intake (AI). It must be careful not to exceed the tolerable upper intake level (UL) of the daily phosphorus intake.

## 4.2. Microminerals

### 4.2.1. Iron

The daily iron intake of Japanese in 2016 was lower compared to that in 1960, 1975, 1980, 1986, 1995, 1998, 2001, 2004, 2007, and 2010 and was the same as that in 2013 (1960: 13.0 mg/day; 1975: 13.4 mg/day; 1980: 10.4 mg/day; 1986:

10.7 mg/day; 1995: 11.8 mg/day; 1998: 11.4 mg/day; 2001: 8.2 mg/day; 2004: 7.9 mg/day; 2007: 7.9 mg/day; 2010: 7.6 mg/day; 2013: 7.4 mg/day; 2016: 7.4 mg/day). In Japanese men and women in 2016, the daily iron intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was 4.4-8.7 mg/day and 4.3-8.1 mg/day, respectively, and was below the tolerable upper intake level (UL) [men (aged  $\geq 1$  year): 25-50 mg/day; women (aged  $\geq 1$  year): 20-40 mg/day] [5]. In Japanese men in 2016, the daily iron intake for men (aged 7-14 years) was 6.9 mg/day and was below the estimated average requirement (EAR) [men (aged 7-14 years): 5.0-8.0 mg/day] [5]. Whereas the daily iron intake for men (aged  $\geq 20$  years) in 2016 was 7.2-8.7 mg/day and was above the estimated average requirement (EAR) [men (aged  $\geq 20$  years): 6.0-6.5 mg/day] [5]. The daily iron intake for men (aged 20-39 years) in 2016 was 7.2-7.3 mg/day and was below the recommended dietary allowance (RDA) [men (aged 20-39 years): 7.5 mg/day] [5]. Whereas the daily iron intake for men (aged  $\geq 50$  years) in 2016 was 8.0-8.7 mg/day and was above the recommended dietary allowance (RDA) [men (aged  $\geq 50$  years): 7.0-7.5 mg/day] and was below the tolerable upper intake level (UL) [men (aged  $\geq 50$  years): 50.0 mg/day] [5]. In Japanese women in 2016, the daily iron intake for women (aged  $\geq 1$  year) and women (aged 10-59 years) was 4.3-8.1 mg/day and 6.5-7.4 mg/day, respectively. The estimated average requirement (EAR) of daily iron intake for women without menstruation (aged  $\geq 1$  year) and women with menstruation (aged 10-64 years) was 3.0-7.0 mg/day and 8.5-10.0 mg/day, respectively, and the recommended dietary allowance (RDA) of daily iron intake for women without menstruation (aged  $\geq 1$  year) and women with menstruation (aged 10-59 years) was 4.5-8.5 mg/day and 10.5-12.0 mg/day, respectively [5]. In healthy men (aged  $\geq 50$  years) and women (aged  $\geq 1$  year), overdose of iron-rich foods and/or supplementation should be avoided so as not to exceed the tolerable upper intake level (UL).

The daily iron intake was negatively correlated with the number of gout patients in 1986-2016 ( $r = -0.909$ ,  $p = 0.000107$ ), with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.966$ ,  $p = 0.00757$ ), and with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.985$ ,  $p = 0.00220$ ). Whereas the daily iron intake did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.614$ ,  $p = 0.271$ ). This result suggests that the correlation of daily iron intake with number of gout patients varies with gender and is stronger in adult men than in adult women.

In an epidemiological study, increased iron intake was associated with decreased serum uric acid (SUA) concentrations [9]. It is possible that iron intake prevent gout through a reduction of SUA concentrations.

From the data of food composition [7, 8], it is important for Japanese men (aged 7-14 years, 20-39 years) and women without and with menstruation (aged  $\geq 1$  year) to eat lean meat and meats (poultry), organ meats (liver), seafood (oysters, sardines, tuna, sweetfish, abalone, clams, firefly squid), potatoes (konjac), nuts (cashew nuts, pistachio nuts, sesame seeds, flaxseeds), grains (white rice, bread, spaghetti), whole

grains (brown rice, Iron-fortified ready-to-eat cereals and breads), mushrooms (wood ear), legumes (kidney beans, white beans, lentils, peas, green peas), seaweed, fruit (raisins, cantaloupes), vegetables (spinach, broccoli, parsley), dairy products (milk, cheese), soy products (tofu), eggs, tea to take in more iron to reach the recommended dietary allowance (RDA). It must be careful not to exceed the tolerable upper intake level (UL) of the daily iron intake in Japanese men (aged  $\geq 50$  years).

#### 4.2.2. Copper

The daily copper intake of Japanese people in 2016 was lower compared to that in 2001, 2004, 2007, 2010, and 2013 (2001: 1.25 mg/day; 2004: 1.19 mg/day; 2007: 1.16 mg/day; 2010: 1.12 mg/day; 2013: 1.12 mg/day; 2016: 1.11 mg/day). In Japanese men and women in 2016, the daily copper intake for men (aged  $\geq 1$  year) and women (aged  $\geq 1$  year) was 0.69-1.30 mg/day and 0.69-1.13 mg/day, respectively, and exceeded the estimated average requirement (EAR) [men (aged  $\geq 1$  year): 0.3-0.8 mg/day; women (aged  $\geq 1$  year): 0.3-0.6 mg/day] and the recommended dietary allowance (RDA) [men (aged  $\geq 1$  year): 0.3-0.9 mg/day; women (aged  $\geq 1$  year): 0.3-0.7 mg/day] [5]. In Japanese men and women in 2016, the daily copper intake for men (aged  $\geq 18$  years) and women (aged  $\geq 18$  years) was 1.14-1.30 mg/day and 0.95-1.13 mg/day, respectively, and was below the tolerable upper intake level (UL) [men (aged  $\geq 18$  years): 7.0 mg/day; women (aged  $\geq 18$  years): 7.0 mg/day] [5]. The Ministry of Health, Labour and Welfare in Japan [5] has not set a tolerable upper intake level (UL) for healthy men and women (aged 0-17 years) because there is no scientific evidence for health problems due to excessive daily intake of copper and has expressed the view that healthy people do not overdose copper in their normal diet, but overdose of copper can occur due to improper use of supplementation. In healthy men and women, taking of copper supplementation should be careful so as not to exceed the tolerable upper intake level (UL). The Ministry of Health, Labour and Welfare in Japan [5] have stated that the daily copper intake of Japanese people in 2016 was appropriate.

The daily copper intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.933$ ,  $p = 0.00652$ ), and with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.925$ ,  $p = 0.0242$ ). The daily copper intake tended to be negatively correlated with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.877$ ,  $p = 0.0511$ ). The daily copper intake tended to be positively correlated with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.878$ ,  $p = 0.0503$ ). This result suggests that the correlation of daily copper intake with the number of gout patients varies with gender.

#### 4.2.3. Zinc

The daily zinc intake of Japanese people in 2016 was lower compared to that in 2001, 2004, and 2007 and was higher compared to that in 2010 and was the same as that in 2013 (2001: 8.5 mg/day; 2004: 8.3 mg/day; 2007: 8.2 mg/day; 2010:

7.9 mg/day; 2013: 8.0 mg/day; 2016: 8.0 mg/day). In Japanese men and women in 2016, the daily zinc intake for men (aged 1-69 years) and women (aged  $\geq 1$  year) was 5.5-10.8 mg/day and 5.3-7.9 mg/day, respectively, and exceeded the estimated average requirement (EAR) [men (aged 1-69 years): 3.0-10.0 mg/day; women (aged  $\geq 1$  year): 2.0-7.0 mg/day] [5]. The daily zinc intake for men (aged  $\geq 70$  years) in 2016 was 8.4 mg/day and was below the estimated average requirement (EAR) [men (aged  $\geq 70$  years): 9.0 mg/day] [5]. In Japanese men and women in 2016, the daily zinc intake for men (1-6 years) and women (aged 1-6 years) was above the recommended dietary allowance (RDA) [men (aged 1-6 years): 3.0-5.0 mg/day; women (aged 1-6 years): 3.0-4.0 mg/day] [5]. In Japanese men and women in 2016, the daily zinc intake for men (aged  $\geq 15$  years) and women (aged  $\geq 15$  years) was below the recommended dietary allowance (RDA) [men (aged  $\geq 15$  years): 10.0-12.0 mg/day; women (aged  $\geq 15$  years): 8.0 mg/day] and the daily zinc intake for men (aged  $\geq 18$  years) and women (aged  $\geq 18$  years) was below the tolerable upper intake level (UL) [men (aged  $\geq 18$  years): 40.0-45.0 mg/day; women (aged  $\geq 18$  years): 30.0-35.0 mg/day] [5]. The Ministry of Health, Labour and Welfare in Japan [5] has not set a tolerable upper intake level (UL) for healthy men and women (aged 0-17 years) because there is no scientific evidence for health problems due to excessive daily intake of zinc and has expressed the view that healthy people do not overdose zinc in their normal diet, but overdose of zinc can occur due to improper use of supplementation.

The daily zinc intake was negatively correlated with the number of gout patients in 2001-2016 ( $r = -0.868$ ,  $p = 0.0205$ ). The daily zinc intake did not show a significant correlation with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.695$ ,  $p = 0.192$ ), with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2016 ( $r = -0.842$ ,  $p = 0.0732$ ), and with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2016 ( $r = 0.821$ ,  $p = 0.0881$ ). This result suggests that the correlation of daily zinc intake with the number of gout patients tends to vary with gender.

In an epidemiological study, increased zinc intake was associated with decreased hyperuricemia risk [45]. It is possible that zinc intake prevent gout through decreased hyperuricemia risk.

Judging from the data of food composition [7, 8], it is important for Japanese people (aged  $\geq 15$  years) to eat meats (beef, chicken), processed meats (beef chuck, beef patty, beef jerky, pork chop), organ meats (liver, breast), seafood (oysters, crab, lobster, blue mackerel, anchovy, sardines, snail, scallop, lamprey), seeds and nuts (pumpkin seeds, cashew nuts, almonds, sesame seeds, flaxseeds, chia seeds), whole grains (fortified ready-to-eat cereals, oatmeal), mushrooms (maitake mushrooms), legumes (kidney beans, baked beans, chickpeas, green peas), seaweed, dairy products (low-fat milk, cheese, yogurt) to take in more zinc to reach the recommended dietary allowance (RDA). It must be careful not to exceed the tolerable upper intake level (UL) of the daily zinc intake in Japanese men (1-6 years) and women (aged 1-6 years).

## 5. Alcohol

The Ministry of Health, Labour and Welfare of Japan [5] has not determined dietary reference intakes for alcohol in Japanese people.

In epidemiological studies, increased intake of alcohol was associated with increased serum uric acid (SUA) concentrations [9, 17, 18, 46-52], hyperuricemia risk [18, 50, 51, 53-66], and gout risk [10, 22, 46, 48, 54, 67-69].

Proposed mechanisms of higher alcohol consumption associated with increased SUA levels and hyperuricemia risk were reviewed in detail by Yamamoto et al. [70] and Koguchi [71]. In brief, alcohol consumption increases uric acid (UA) liver production through ATP degradation, leading to accumulation of ADP and AMP [72], and it increases lactic acid production, which has a competitive inhibitory effect on UA excretion and ethanol can increase the rate of sputum synthesis in humans and increase UA production [73]. In addition, alcohol consumption leads to dehydration and metabolic acidosis, resulting in decreased UA excretion [74]. Heavy alcohol (ethanol) consumption increases the production of UA, which resulted in increases in SUA concentration and urinary UA excretion, leads to hyperuricemia [70].

Excessive alcohol consumption was associated with increased risk of gout attacks [64, 75]. All forms of alcohol promote gout flares when ingested in a condensed period of time (e.g., more than three servings in a 24-hour period) [76]. Terkeltaub and Edwards [76] have stated that the patient can help lessen gout flares by moderating food portion sizes and content, by not drinking alcohol in excess in short time periods, and by staying well hydrated (five or eight 250-mL servings of water daily unless medically contraindicated).

The guidelines recommended the following for alcohol consumption: (1) limit alcohol consumption for patients with gout [27, 77]; (2) reduced consumption of alcohol (particularly beer, but also wine and spirits) and avoidance of alcohol overuse (defined as more than 2 servings per day for a male and 1 serving per day for a female) in all gout patients [35]; (3) avoidance of alcohol (especially beer and spirits) for patients with gout [78]; (4) in patients with hypertension, limit alcohol consumption [2 standard drinks for men and 1.5 for women (10 g alcohol/standard drink)] [38] or limit ethanol consumption ( $\leq 20$ -30 mL/day for men and  $\leq 10$ -20 mL/day for women) [39]; (5) avoidance of binge drinking for patients with hypertension [38]; (6) moderation of alcohol consumption (no more than two drinks per day for adult men and no more than one drink per day for adult women) for patients with diabetes mellitus [34]; (7) alcohol intake for patients with diabetes mellitus ( $< 25$  g/day) [40]; and (8) circadian drinking for patients with urolithiasis [36]. World Health Organization (WHO) [42] have indicated that many studies have shown a U- or J-shaped association between mortality and alcohol consumption, in which people who drink light or moderate amounts have a lower death rate than non-drinkers, while those who drink large amounts have a higher death rate.

## 6. Conclusion

In this article, the author suggested the importance of micronutrient (vitamin and mineral) intake and alcohol consumption for prevention of gout in Japanese people referencing the results of clinical research reported. Japanese people (aged  $\geq 15$  years) should take in more vitamin A, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, calcium, potassium, magnesium, and zinc to reach the recommended dietary allowance (RDA). In a clinical trial, heavy alcohol (ethanol) consumption increased SUA concentration and decreased urinary UA excretion, led to hyperuricemia [70]. Many epidemiological studies reported the association between dietary factors and SUA concentrations [9, 17, 18, 46-52], hyperuricemia risk [18, 50, 51, 53-66], or gout risk [10, 22, 46, 48, 54, 67-69]. Limiting alcohol consumption seems to be important for the prevention of gout in Japanese adult people.

Modification of nutrient intake for the prevention of gout in Japanese people (especially adults) involving the view in the previous report [2] are as follows: energy-providing nutrient balance (percentages of proteins, fats, and carbohydrates of total energy intake) should be within the range of the tentative dietary goal for preventing lifestyle-related diseases (DG); reduce fat (especially animal fat) intake and maintain the mean ratio of energy intake from saturated fatty acids in total energy intake (Saturated fatty acids/Energy) within the range of the tentative dietary goal for preventing lifestyle-related diseases (DG); replacement of saturated fatty acids with mono- and polyunsaturated ones (especially n-3 polyunsaturated fatty acids); avoidance of excessive intake of saturated fatty acids and cholesterol; limiting or decreasing salt intake; pay attention to sucrose and fructose intake; increase intake of dietary fiber, vitamin A, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, calcium, potassium, magnesium, and zinc; and maintenance of good hydration. It is necessary to recognize what food intake is important for the prevention of gout in Japanese people.

## Conflict of Interest Statement

The author declares that there are no conflicts of interest.

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