

# Modification of Animal Product Intake for Prevention of Gout in Japanese People in 2019:2022 Update

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**Abstract:** The number of patients with gout has been increasing in Japan. A previous report showed modification of dietary habits for the prevention of gout in Japanese people in 2016 through the trends in food intake of Japanese people in 1946-2016. The aim of this article is to suggest what food intake is important for the prevention of gout in Japanese people in 2019 referencing the results of clinical research reported. As the previous report, the author used the data of the Comprehensive Survey of Living Conditions in Japan for the number of gout patients (1986-2019) and the data of the National Health and Nutrition Survey in Japan (1946-2019) for the intake of foods. Food intake of Japanese people in 2019 was compared with that in 2016. The relationship between the number of gout patients and food intake in Japanese people was examined. The daily intake of total animal products, total meat, eggs, oils and fats, and alcoholic beverages of Japanese people in 2019 were higher compared to those in 2016, respectively. Whereas the daily intake of total seafood (fish and shellfish), milk and dairy products, seasonings, condiments and spices, and confectioneries of Japanese people in 2019 were lower compared to those in 2016, respectively. The significance of the correlation between the number of gout patients and intake of total meat, total seafood, eggs, seasonings, condiments and spices, oils and fats, confectioneries, or alcoholic beverages in 1986-2016 were also observed that in 1986-2019. Modification of intake of animal products, seasonings, condiments and spices, confectioneries, and beverages for the prevention of gout in Japanese people in 2019 is suggested as follows: limiting intake of meat; limiting alcohol beverage consumption; limiting or decreasing intake of salt, oils and fats, and confectioneries; avoidance of excessive intake of sugar-sweetened beverages and sugary foods including desserts and sweets; increasing the intake of milk and dairy products (particularly low-fat dairy products).

**Keywords:** Alcoholic Beverage, Animal Product, Food, Gout, Hyperuricemia, Nutrient, Uric Acid

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## 1. Introduction

Uric acid (UA) is the primary antioxidant in human plasma and accounts for more than 60% of the capacity to scavenge free oxidative radicals in the serum [1]. The antioxidant activity of UA is overcome by the pro-oxidant and proinflammatory effects of reactive oxygen species accumulation under ischemic conditions [2]. The pro-oxidant and proinflammatory effects are the result of the accumulation of oxygen free radicals after xanthine dehydrogenase (EC1.17.1.4) converts to xanthine oxidase (EC1.17.3.2) in parallel with UA production as an effect of adenosine triphosphate degradation [3]. UA can oxidize low-density lipoprotein (LDL) in the presence of copper ions and lipid hydroperoxides, increasing the inflammatory status [4]. The

SUA concentrations have been associated with several inflammatory markers [neutrophil count, C-reactive protein, interleukin-1 receptor antagonist (IL-1ra), interleukin-6 (IL-6), interleukin-18 (IL-18), tumor necrosis factor-alpha (TNF- $\alpha$ )] in individuals with or without hyperuricemia [SUA concentration > 7.5 mg/dL (450  $\mu$ mol/L) in men and > 6.2 mg/dL (372  $\mu$ mol/L) in women] [5]. The anti-inflammatory effect is mediated through the regulation of various inflammatory cytokines [e.g., nitric oxide, interleukins, tumor necrosis factor-alpha (TNF- $\alpha$ ), interferon gamma] or noncytokine mediator (e.g., prostaglandin E<sub>2</sub>) [6]. Prostaglandins are inflammatory instigators whose production is mediated by cyclooxygenases (COXs) and are

produced as a result of crystal-induced inflammation [7]. Phytochemicals from fruit, vegetables, and food legumes have anti-inflammatory effects in *in vitro* and animal model studies [6]. Recent studies have illustrated that phytochemicals with potent antioxidant activity exert inhibitory effect on the nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome-mediated diseases, such as central nervous system diseases (i.e., Parkinson's disease, Alzheimer's disease, depression), metabolic disorders (i.e., obesity, type 1 and type 2 diabetes mellitus), chronic inflammatory diseases (i.e., colitis, arthritis, gouty arthritis) [8-10].

The prevalence of gout in Japan has increased markedly since the 1960s because of the westernization of the Japanese diet from 1955 [11]. Recently, the Ministry of Health, Labour and Welfare in Japan [12-15] has shown the number of gout patients and the intake of nutrients or foods in 2019. The number of gout patients of Japanese people in 2019 was higher compared to that in 2016 and increased 4.92-fold compared to that in 1986 (1986: 0.255 million; 2016: 1.105 million; 2019: 1.254 million) [12].

To explore means of the dietary control for the prevention of gout, the author [11, 16-20] has proposed the modification of nutrient intake for the prevention of gout in Japanese people in 2016 and 2019. Modification of nutrient intake for the prevention of gout in Japanese people in 2019 is suggested as described below: reduce the mean ratio of energy intake from saturated fatty acids in total energy intake (Saturated fatty acids/Energy); limiting or decreasing intake of fat (particularly animal fat), saturated fatty acids, cholesterol, and salt; decreasing intake of phosphorus and copper; increase intake of carbohydrate (particularly dietary fiber), vitamin A, vitamin E, vitamin B<sub>1</sub>, vitamin B<sub>6</sub>, folate, vitamin B<sub>12</sub>, calcium, potassium, magnesium, and zinc; increase intake of vitamin B<sub>2</sub> and vitamin C in Japanese men (aged 20-59 years) and women (aged 20-59 years). In addition, the important points of macronutrient intake for the prevention of gout in Japanese people (especially adults) is suggested as follows: The percentage of carbohydrate, protein, fat, and n-3 polyunsaturated fatty acids and n-6 polyunsaturated fatty acids in total energy intake should be within the range of the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan or the Acceptable Macronutrient Distribution Ranges (AMDRs) set by the Institute of Medicine of the National Academy of Sciences in the U.S.; 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) established by the Ministry of Health, Labour and Welfare in Japan; recognizing increased intake of dietary fiber, animal sources of protein (e.g., casein, lactalbumin), and vegetable sources of protein (e.g., wheat gluten, rice endosperm protein); avoidance of excessive intake of saturated fatty acids and cholesterol; replacement of saturated fatty acids (e.g., dairy fats, meat fat) with mono- and

polyunsaturated fatty acids (particularly n-3 polyunsaturated fatty acids) (e.g., macadamia nuts, almonds, peanuts and peanut butter, olive oil, canola oil, avocados); pay attention to not to excessive intake of sugars (particularly fructose and sucrose); limiting alcohol consumption; and maintenance of good hydration; recognizing intake of vitamin D, vitamin E, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, folate, vitamin B<sub>12</sub>, vitamin C, calcium, magnesium, iron, and zinc; and pay attention to intake of salt [19, 20].

From the results of the previous reports [19, 20], it is necessary to recognize what food intake is important for Japanese people to prevent gout. This article shows the relationship between the number of gout patients and intake of animal products, seasonings, condiments and spices, confectioneries, or beverages in Japanese people in 2019 and suggests modification of the above food intake for the 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 (1986-2019) [12]. 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 2019 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 (1946-2019) performed by the Ministry of Health, Labour and Welfare in Japan [13-15].

Data were extracted from the series of Japanese National Nutrition Surveys that have been carried out every year throughout Japan since 1946 [15]. 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 (1946-2019) [13].

### 2.3. 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 [21] and the National Institutes of Health in the U.S. Department of Health & Human Services [22].

## 2.4. Statistical Analysis

The correlation efficient and the significance of the correlation between the number of gout patients and food intake in 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 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 Animal Product Intake in Japanese People

The results on the correlation between the number of gout patients and food intake in Japanese people are shown in Tables 1 and 2. Tables 1 and 2 showed that the significance of the correlation between the number of gout patients and food intake in 1986-2016 were also observed that in 1986-2019.

**Table 1.** Correlation between number of gout patients and intake of food group in Japanese people in 1986-2016 and 1986-2019.

Food group	Year	1986-2016*		1986-2019	
		coefficient	p-value	coefficient	p-value
Animal Products		- 0.412	0.208	- 0.349	0.266
Meat		0.805	0.003	0.843	< 0.001
Seafood		- 0.884	< 0.001	- 0.911	< 0.001
Eggs		- 0.937	< 0.001	- 0.731	0.007
Milk and Dairy Products		- 0.036	0.917	0.032	0.921
Seasonings, Condiments, and Spices		-0.905	< 0.001	-0.919	< 0.001
Oils and Fats		- 0.928	< 0.001	- 0.892	< 0.001
Confectioneries		0.711	0.014	0.670	0.017
Alcoholic Beverages		0.861	< 0.001	0.873	< 0.001

\* Adapted from Koguchi [18].

**Table 2.** Correlation between number of gout patients and food item intake in Japanese people in 1986-2016 and 1986-2019.

Food	Year	1986-2016**		1986-2019	
		coefficient	p-value	coefficient	p-value
Meat					
Pork		0.886	< 0.001	0.913	< 0.001
Poultry		0.838	0.001	0.848	< 0.001
Ham and Sausage		0.949	< 0.001	0.960	< 0.001
Beef		- 0.629	0.038	- 0.606	0.037
Wheal Meat		- 0.406	0.216	- 0.346	0.271
Seafood					
Raw Fish		- 0.883	< 0.001	- 0.911	< 0.001
Raw Seafood		- 0.894	< 0.001	- 0.919	< 0.001
Shellfish		- 0.710	0.014	- 0.747	0.005
Seafood Processed Foods		- 0.702	0.016	- 0.754	0.005
Milk and Dairy Products					
Cheese		0.932	< 0.001	0.926	< 0.001
Milk		- 0.901	< 0.001	- 0.913	< 0.001
Seasonings, Condiments, and Spices					
Salt*		- 0.903	< 0.001	- 0.913	< 0.001
Soy Sauce		- 0.905	< 0.001	- 0.919	< 0.001
Sauce		- 0.917	< 0.001	- 0.914	< 0.001
Mayonnaise		- 0.898	< 0.001	- 0.854	< 0.001
Oils and Fats					
Margarine		- 0.850	< 0.001	- 0.873	< 0.001
Vegetable Oils and Fats		- 0.856	< 0.001	- 0.760	0.004
Animal Oils and Fats		- 0.643	0.033	- 0.421	0.173
Butter		- 0.0445	0.897	0.0385	0.905
Confectioneries					
Jam		0.617	0.043	0.657	0.020
Alcoholic Beverages					
Beer		0.695	0.018	0.702	0.011
Rice Wine		- 0.929	< 0.001	- 0.946	< 0.001
Other Liquors		0.967	< 0.001	0.974	< 0.001

\* Adapted from Koguchi [17, 20]. \*\* Adapted from Koguchi [18].

### 3.1. Animal Products

The daily intake of total animal products of Japanese people

in 2019 was higher compared to that in 2016 (2016: 329.7 g/day; 2019: 340.1 g/day). The daily intake of total animal products of Japanese people did not show a significant

correlation with the number of gout patients in 1986-2019 ( $r = -0.349$ ,  $p = 0.266$ ).

### 3.2. Meat

The daily total meat intake of Japanese people in 2019 was higher compared to that in 2016 (2016: 95.5 g/day; 2019: 103.0 g/day). The daily intake of total meat of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r = 0.843$ ,  $p = 0.000569$ ).

The daily intake of total meat of Japanese adult people (aged  $\geq 20$  years), Japanese adult men (aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were higher compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 93.0 g/day; 2019: 101.0 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 109.1 g/day; 2019: 117.4 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 79.6 g/day; 2019: 86.7 g/day]. In Japanese adult people (aged  $\geq 20$  years) or Japanese adult men (aged  $\geq 20$  years), the daily total meat intake was positively correlated with the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r = 0.974$ ,  $p = 0.000997$ ; Japanese adult men (aged  $\geq 20$  years):  $r = 0.972$ ,  $p = 0.00114$ ]. Whereas the daily total meat intake of Japanese adult women (aged  $\geq 20$  years) did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2019 ( $r = -0.555$ ,  $p = 0.253$ ). This result suggests that the correlation of daily total meat intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily beef intake of Japanese people in 2019 was higher compared to that in 2016 (2016: 14.3 g/day; 2019: 15.2 g/day). The daily beef intake of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.606$ ,  $p = 0.0368$ ).

The daily intake of pork, poultry, ham and sausage of Japanese people in 2019 were higher compared to those in 2016, respectively (pork: 2016: 39.5 g/day; 2019: 40.5 g/day; poultry: 2016: 27.0 g/day; 2019: 32.4 g/day; ham and sausage: 2016: 12.9 g/day; 2019: 13.4 g/day). The daily intake of pork, poultry, and ham and sausage of Japanese people were positively correlated with the number of gout patients in 1986-2019, respectively (pork:  $r = 0.913$ ,  $p = 0.0000342$ ; poultry:  $r = 0.848$ ,  $p = 0.000495$ ; ham and sausage:  $r = 0.960$ ,  $p = 0.000000719$ ).

The daily wheal meat intake of Japanese people in 2019 was the same as that in 2016 (2016: 0.1 g/day; 2019: 0.1 g/day). The daily wheal meat intake of Japanese people did not show a significant correlation with the number of gout patients in 1986-2019 ( $r = -0.346$ ,  $p = 0.271$ ).

The daily intake of organ meats of Japanese people in 2019 was lower compared to that in 2016 (2016: 1.4 g/day; 2019: 1.3 g/day). The daily intake of organ meats of Japanese people did not show a significant correlation with the number of gout patients in 2001-2019 ( $r = -0.522$ ,  $p = 0.230$ ).

Meat intake increased plasma uric acid (PUA) or serum uric acid (SUA) concentrations in normal human subjects [23]. In epidemiological studies, increased meat intake was associated

with increased SUA concentrations [24-33], hyperuricemia risk [32, 34-40], and gout risk [27, 28, 31, 35, 41-44]. In a prospective cohort study, higher intake of red meat and poultry were associated with increased gout risk, respectively [45]. Consumption of red meat is low, because limiting intake of red meat would reduce SUA levels [46]. Excessive intake of meat was associated with increased risk of gout attacks [47, 48]. These results suggest that decrease in daily meat intake in Japanese people is essential for the prevention and suppression of gout.

The guidelines recommended the following for meat intake in patients with gout: (1) avoidance of excessive intake of meat [49]; (2) reduce red meat intake and avoiding offal intake [50]; and (3) limit purine-rich meat intake and avoidance of organ meats high in purine content (e.g., sweetbreads, liver, kidney) [51].

### 3.3. Seafood

The daily intake of total seafood (fish and shellfish) of Japanese people in 2019 was lower compared to that in 2016 (2016: 65.6 g/day; 2019: 64.1 g/day). The daily intake of total seafood of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.911$ ,  $p = 0.0000370$ ).

The daily intake of total seafood of Japanese adult people (aged  $\geq 20$  years), Japanese adult men (aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were lower compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 70.5 g/day; 2019: 68.5 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 78.0 g/day; 2019: 76.3 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 64.3 g/day; 2019: 61.7 g/day]. In Japanese adult people (aged  $\geq 20$  years) or Japanese adult men (aged  $\geq 20$  years), the daily intake of total seafood was negatively correlated with the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r = -0.929$ ,  $p = 0.00737$ ; Japanese adult men (aged  $\geq 20$  years):  $r = -0.948$ ,  $p = 0.00392$ ]. Whereas the daily intake of total seafood of Japanese adult women (aged  $\geq 20$  years) was positively correlated with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2019 ( $r = 0.838$ ,  $p = 0.0372$ ). This result suggests that the correlation of daily intake of total seafood with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The daily intake of raw seafood of Japanese people in 2019 was lower compared to that in 2016 (2016: 39.4 g/day; 2019: 37.4 g/day). The daily intake of raw seafood of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.919$ ,  $p = 0.0000233$ ).

The daily intake of seafood processed foods and shellfish of Japanese people in 2019 were higher compared to those in 2016, respectively (seafood processed foods: 2016: 26.2 g/day; 2019: 26.6 g/day; shellfish: 2016: 2.2 g/day; 2019: 2.8 g/day). The daily intake of seafood processed foods and shellfish of Japanese people were negatively correlated with the number of gout patients in 1986-2019, respectively (seafood processed foods:  $r = -0.754$ ,  $p = 0.00464$ ; shellfish:  $r = -0.747$ ,  $p = 0.00524$ ).

The daily intake of shrimp and crab of Japanese people in 2019 was higher compared to that in 2016 (2016: 3.4 g/day; 2019: 3.5 g/day). The daily intake of shrimp and crab of Japanese people was negatively correlated with the number of gout patients in 2001-2019 ( $r = -0.925$ ,  $p = 0.00287$ ).

The daily intake of squid and octopus of Japanese people in 2019 was lower compared to that in 2016 (2016: 3.2 g/day; 2019: 3.0 g/day). The daily intake of squid and octopus of Japanese people was negatively correlated with the number of gout patients in 2001-2019 ( $r = -0.970$ ,  $p = 0.000299$ ).

The daily intake of raw fish of Japanese people in 2019 was lower compared to that in 2016 (2016: 39.4 g/day; 2019: 37.4 g/day). The daily intake of raw fish of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.911$ ,  $p = 0.0000377$ ).

Fish intake increased plasma uric acid (PUA) or serum uric acid (SUA) concentrations in normal human subjects [23]. In epidemiological studies, increased intake of seafood (including fish and shellfish) was associated with increased SUA concentrations [24, 28, 32, 33], hyperuricemia risk [32, 35, 36, 38, 40, 52-55], and gout risk [28, 35, 44, 45]. These results suggest that decrease in daily seafood (including fish and shellfish) intake in Japanese people is essential for the prevention of gout. Intake of shrimp and shell, which are purine-rich foods, in hyperuricemic patients was an independent risk factor for gout development from hyperuricemia [56].

In an internet-based case-crossover study of U.S. adults (aged  $\geq 19$  years) with preexisting gout, subjects who consumed n-3 polyunsaturated fatty acids (PUFA)-rich fish during the preceding 48 hours had a 33% lower risk of recurrent gout flare compared with those who did not [adjusted OR = 0.77, (95% confidence interval, 0.61-0.96),  $p = 0.02$ ] [57]. Moreover the highest tertile of n-3 polyunsaturated fatty acids (PUFA)-rich fish intake ( $\geq 2$  servings) was 26.0% reduced risk of recurrent gout flare compared with the lowest tertile of polyunsaturated fatty acids (PUFA)-rich fish intake (0 servings) in adjusted model, which is adjusted for alcohol consumption, total purine intake, diuretic use and other urate-lowering or flare prophylactic medications (allopurinol, non-steroidal anti-inflammatory drugs, colchicine) [adjusted OR = 0.74, (95% confidence interval, 0.54-0.99),  $p = 0.04$ ] [57]. However, Zhang et al. [57] have stated that fatty fish is not ideal source of n-3 polyunsaturated fatty acids (PUFA) due to its concomitant purines. Purine-rich foods include seafood (i.e., fish fillets, tuna, mackerel, salmon, shrimp, lobster, clams, etc.) [58, 59]. Tuna, mackerel, and salmon, which are fatty fish, also contains rich in n-3 polyunsaturated fatty acids [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] [21, 22]. It seems better to take in n-3 polyunsaturated fatty acids (PUFA)-rich fish (especially tuna, mackerel, and salmon).

The guidelines recommended the following for seafood intake in patients with gout: (1) avoidance of excessive intake of seafood [49]; (2) avoidance of intake of offal and shellfish [50]; and (3) limit purine-rich seafood intake and avoidance of

organ meats high in purine content (e.g., sweetbreads, liver, kidney) [51].

Hisatome et al. [58] have recommended that intake of fish, shellfish, prawn and shrimp, and crab per one serving should be 80 g and  $\leq 60$  g,  $\leq 50$  g, and 100g, respectively. The daily total seafood (fish and shellfish) intake of Japanese people in 2019 (64.1 g/day) was less than the recommended intake of fish or crab per one serving by Hisatome et al. [58]. From the data of food composition [21, 22], it is important for Japanese people to eat seafood to take in more vitamin A, vitamin D, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, pantothenic acid, folate, calcium, potassium, magnesium, phosphorus, iron, and zinc. The guidelines have recommended that eating foods rich in long-chain n-3 polyunsaturated fatty acids, such as fatty fish, which contains eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is recommended to prevent or treat cardiovascular disease (CVD) [60, 61]. Terkeltaub and Edwards [62] have stated that seafood (especially shellfish and crustaceans) consumption for hyperuricemia and gout patients should be  $\leq 6$  oz (170 g) per day as a starting point. Higher intake of seafood was associated with increased gout risk [28, 35, 44]. The daily intake of total seafood of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.911$ ,  $p = 0.0000370$ ). Therefore, the daily seafood (especially fish and fatty fish) intake reaching 80 g seems to be needed, as Hisatome et al. [58] have recommended.

### 3.4. Eggs

The daily egg intake of Japanese people in 2019 was higher compared to that in 2016 (2016: 35.6 g/day; 2019: 40.4 g/day). The daily egg intake of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r = -0.731$ ,  $p = 0.00687$ ).

The daily egg intake of Japanese adult people (aged  $\geq 20$  years), Japanese adult men (aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were higher compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 36.3 g/day; 2019: 41.4 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 38.9 g/day; 2019: 43.5 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 34.1 g/day; 2019: 39.4 g/day]. The daily egg intake of Japanese adult people (aged  $\geq 20$  years) tended to be positively correlated with the number of gout patients in the adult population (aged  $\geq 20$  years) in 2004-2019 ( $r = 0.783$ ,  $p = 0.653$ ). In Japanese adult men (aged  $\geq 20$  years) or Japanese adult women (aged  $\geq 20$  years), there was no significant correlation between the daily egg intake and the number of gout patients in 2004-2019 [Japanese adult men (aged  $\geq 20$  years):  $r = 0.755$ ,  $p = 0.0845$ ; Japanese adult women (aged  $\geq 20$  years):  $r = -0.466$ ,  $p = 0.351$ ].

In epidemiological studies, increased egg intake was associated with decreased serum uric acid (SUA) concentrations [25, 27] and hyperuricemia risk [63]. This result suggests that increase in daily egg intake in Japanese people is essential for the prevention of gout through reduced SUA concentrations and decreased hyperuricemia risk. Considering the mean ratio of energy intake from protein in

total energy intake (Protein/Energy) and the daily vitamin A, vitamin D, vitamin B<sub>1</sub>, pantothenic acid, folate, phosphorus, iron intake, the daily egg intake seems to be appropriate or it seems better to increase it slightly.

### 3.5. Milk and Dairy Products

The daily intake of milk and dairy products of Japanese people in 2019 was lower compared to that in 2016 (2016: 131.8 g/day; 2019: 131.2 g/day). The daily intake of milk and dairy products of Japanese people did not show a significant correlation with the number of gout patients in 1986-2019 ( $r=0.0319$ ,  $p=0.921$ ).

The daily intake of milk and dairy products of Japanese adult people (aged  $\geq 20$  years) and Japanese adult women (aged  $\geq 20$  years) in 2019 were lower compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 111.2 g/day; 2019: 110.7 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 120.3 g/day; 2019: 117.4 g/day]. The daily intake of milk and dairy products of Japanese adult men (aged  $\geq 20$  years) in 2019 was higher compared to that in 2016 (2016: 100.2 g/day; 2019: 103.1 g/day). In Japanese adult people (aged  $\geq 20$  years) or Japanese adult men (aged  $\geq 20$  years), the daily intake of milk and dairy products tended to be positively correlated with the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r=0.777$ ,  $p=0.0693$ ; Japanese adult men (aged  $\geq 20$  years):  $r=0.784$ ,  $p=0.0647$ ]. The daily intake of milk and dairy products of Japanese adult women (aged  $\geq 20$  years) did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2019 ( $r=-0.141$ ,  $p=0.790$ ).

The daily intake of milk of Japanese people in 2019 was lower compared to that in 2016 (2016: 81.8 g/day; 2019: 81.6 g/day). The daily milk intake of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r=-0.913$ ,  $p=0.0000337$ ).

The daily intake of yoghurt and fermented milk drink of Japanese people in 2019 was lower compared to that in 2016 (2016: 38.4 g/day; 2019: 36.8 g/day). The daily intake of yoghurt and fermented milk drink of Japanese people was positively correlated with the number of gout patients in 2001-2019 ( $r=0.897$ ,  $p=0.00618$ ).

The daily cheese intake of Japanese people in 2019 was higher compared to that in 2016 (2016: 3.2 g/day; 2019: 3.9 g/day). The daily cheese intake of Japanese people was positively correlated associated with the number of gout patients in 1986-2019 ( $r=0.926$ ,  $p=0.0000153$ ).

Milk [64] and dairy products [64-68] decreased serum uric acid (SUA) concentrations. In epidemiological studies, increased intake of dairy products was associated with decreased SUA concentrations [24-27, 29, 30, 32, 66, 69] and hyperuricemia risk [27, 32, 35, 43, 69]. This result suggests that increase in daily dairy product intake in Japanese people is essential for the prevention of gout through reduced SUA concentrations and decreased hyperuricemia risk.

The ingestion of milk proteins (casein, lactalbumin) and orotic acid has been shown to exert a uricosuric effect in

healthy subjects [70]. Milk ingested promote renal oxypurine excretion, thereby reducing the availability of precursor substrates necessary for urate production [64, 67, 71].

In a randomized controlled trial, skimmed milk powder derivatives (glycomacropeptide and G600 milk fat extract) have anti-inflammatory effects against acute gout flares [72]. Skim milk enriched with glycomacropeptide and G600 milk fat extract found a small reduction in the frequency of gout flares [70, 72]. The use of skimmed milk powder enriched with two dairy fractions (glycomacropeptide and G600 fat extract) did not result in a reduction in frequency of acute gout flares when standard skimmed milk or lactose powder [72].

The guidelines recommended encourage intake of low-fat dairy products or nonfat dairy products for patients with gout [49-51].

The Ministry of Health, Labour and Welfare in Japan has recommended that the daily dairy product intake must be 130 g or more [14]. The Dietary guidelines for Japanese (The Japanese food guide spinning top) has recommended that the daily consumption of milk and milk products must be 2-3 servings (milk: approximately 100 g/serving; yogurt: approximately 83 g/serving; cheese: approximately 20 g/serving), depending on an individual's caloric intake [73]. The daily milk and dairy product intake of Japanese people in 2019 was 131.2 g. The daily milk and dairy product intake did not show a significant correlation with the number of gout patients in 1986-2019 ( $r=0.0319$ ,  $p=0.921$ ). Higher intake of dairy products [35, 42-44] and low-fat dairy products [41] were associated with decreased gout risk, respectively. This result suggests that increase in daily intake of milk and dairy products (especially low-fat dairy products) in Japanese people is essential for the prevention of gout. Considering the result from the balance of the caloric ratio of protein, fat and carbohydrate in Japanese people in 2019 (protein: 15.1%, fat: 28.6%, and carbohydrate: 56.3%) and the daily vitamin A, vitamin D, vitamin B<sub>1</sub>, vitamin B<sub>2</sub>, vitamin B<sub>6</sub>, pantothenic acid, folic acid, calcium, magnesium, phosphorus, iron, zinc, purine intake, it is important for Japanese people to eat low-fat dairy products. The daily intake of milk and dairy products (especially low-fat dairy products) seems to be appropriate or it seems better to increase it slightly.

## 4. Relationship Between the Number of Gout Patients and Intake of Seasonings or Oils and Fats in Japanese People

### 4.1. Seasonings, Condiments and Spices

The daily intake of seasonings, condiments and spices of Japanese people in 2019 was lower compared to that in 2016 (2016: 93.2 g/day; 2019: 62.5 g/day). The daily intake of seasonings, condiments, and spices of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r=-0.919$ ,  $p=0.0000235$ ).

The daily intake of seasonings, condiments, and spices of Japanese adult people (aged  $\geq 20$  years), Japanese adult men

(aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were lower compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 98.1 g/day; 2019: 64.9 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 108.9 g/day; 2019: 70.3 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 89.1 g/day; 2019: 60.3 g/day]. In Japanese adult people (aged  $\geq 20$  years) or Japanese adult men (aged  $\geq 20$  years), the daily intake of seasonings, condiments, and spices tended to be negatively correlated with the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r = -0.799$ ,  $p = 0.0564$ ; Japanese adult men (aged  $\geq 20$  years):  $r = -0.804$ ,  $p = 0.0536$ ]. The daily intake of seasonings, condiments, and spices of Japanese adult women (aged  $\geq 20$  years) did not show a significant correlation with the number of gout patients in adult women (aged  $\geq 20$  years) in 2004-2019 ( $r = 0.402$ ,  $p = 0.430$ ).

The daily intake of soy sauce of Japanese people in 2019 was lower compared to that in 2016 (2016: 12.3 g/day; 2019: 11.7 g/day). The daily intake of soy sauce of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.919$ ,  $p = 0.0000235$ ).

The daily sauce intake of Japanese people in 2019 was lower compared to that in 2016 (2016: 1.8 g/day; 2019: 1.7 g/day). The daily intake of sauce of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.914$ ,  $p = 0.0000317$ ).

The daily mayonnaise intake of Japanese people in 2019 was higher compared to that in 2016 (2016: 2.9 g/day; 2019: 3.4 g/day). The daily intake of mayonnaise of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.854$ ,  $p = 0.000411$ ).

Soy paste (miso) contains polyphenols that suppress uric acid (UA) production by inhibition of xanthine oxidase activity [74]. However, the amount of salt contained in the soy paste (miso), soy sauce, and sauce was 9.7 g/100g, 12.8 g/100g and 5.6-8.5 g/100g, respectively [21]. It seems necessary to decrease the daily intake of soy paste (miso), soy sauce, and sauce in order to reduce the daily salt intake.

The amount of fat contained in the mayonnaise is 9.04 g/100g [21]. Considering the mean ratio of energy intake from fat in total energy intake (Fat/Energy), the daily mayonnaise intake seems to be appropriate or it seems better to decrease.

Spices (capers, caraways, cloves, cumin) contain polyphenols that suppress UA production by inhibition of xanthine oxidase activity [74]. It seems important to cook dishes using above spices in order to maintain serum uric acid (SUA) concentrations at normal levels in healthy people.

The 2012 American College of Rheumatology (ACR) Guidelines for Management of Gout [51] have recommended limiting intake of sauces and gravies in all gout patients. The British Society for Rheumatology Guidelines for the Management of Gout [50] has recommended avoiding yeast extract intake for patients with gout.

#### 4.2. Oils and Fats

The daily intake of oils and fats of Japanese people in 2019 was higher compared to that in 2016 (2016: 10.9 g/day; 2019:

11.2 g/day). The daily intake of oils and fats of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.892$ ,  $p = 0.0000949$ ).

The daily intake of butter of Japanese people in 2019 was higher compared to that in 2016 (2016: 1.0 g/day; 2019: 1.1 g/day). The daily butter intake of Japanese people did not show a significant correlation with the number of gout patients in 1986-2019 ( $r = 0.0385$ ,  $p = 0.905$ ).

The daily intake of vegetable oils and fats of Japanese people in 2019 was higher compared to that in 2016 (2016: 8.7 g/day; 2019: 8.8 g/day). The daily intake of vegetable oils and fats of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.760$ ,  $p = 0.00410$ ).

The daily intake of margarine of Japanese people in 2019 was lower compared to that in 2016 (2016: 1.1 g/day; 2019: 1.0 g/day). The daily intake of margarine of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r = -0.873$ ,  $p = 0.000208$ ).

The daily intake of animal oils and fats of Japanese people in 2019 was the same as that in 2016 (2016: 0.2 g/day; 2019: 0.2 g/day). The daily intake of animal oils and fats of Japanese people did not show a significant correlation with the number of gout patients in 1986-2019 ( $r = -0.421$ ,  $p = 0.173$ ).

Compared to the ideal balance of the caloric ratio of protein, fat, and carbohydrate of Japanese people (protein: 15%, fat: 25%, and carbohydrates: 60%) [75], the balance in Japanese people in 2019 was weighted toward fat (protein: 15.1%, fat: 28.6%, and carbohydrates: 56.3%). The daily intake of oils and fats seems better to decrease until the mean ratio of energy intake from fat in total energy intake (Fat/Energy) becomes 25%.

## 5. Relationship Between the Number of Gout Patients and Confectionery Intake in Japanese People

The daily intake of confectioneries of Japanese people in 2019 was lower compared to that in 2016 (2016: 26.3 g/day; 2019: 25.6 g/day). The daily intake of confectioneries of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r = 0.670$ ,  $p = 0.0172$ ).

The daily intake of confectioneries of Japanese adult people (aged  $\geq 20$  years) and Japanese adult women (aged  $\geq 20$  years) in 2019 were lower compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 24.9 g/day; 2019: 24.4 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 27.6 g/day; 2019: 26.8 g/day]. In Japanese adult people (aged  $\geq 20$  years) or Japanese adult women (aged  $\geq 20$  years), there was no significant correlation between the daily intake of confectioneries and the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r = 0.724$ ,  $p = 0.104$ ; Japanese adult women (aged  $\geq 20$  years):  $r = 0.129$ ,  $p = 0.808$ ]. The daily intake of confectioneries of Japanese adult men (aged  $\geq 20$  years) in 2019 was higher compared to that in 2016 (2016: 21.6 g/day; 2019: 21.7 g/day). The daily intake of confectioneries of

Japanese adult men (aged  $\geq 20$  years) was positively correlated with the number of gout patients in adult men (aged  $\geq 20$  years) in 2004-2019 ( $r=0.819$ ,  $p=0.0464$ ). This result suggests that the correlation of daily confectioneries intake with the number of gout patients tends to be stronger in adult men than in adult women.

The daily jam intake of Japanese people in 2019 was the same as that in 2013 and 2016 (2016: 1.3 g/day; 2019: 1.3 g/day). The daily jam intake of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r=0.657$ ,  $p=0.0203$ ). It seems that decrease in daily intake of confectioneries and jam in Japanese people is essential for the prevention of gout.

Chocolates and cocoa powders contain polyphenols that suppress uric acid (UA) production by inhibition of xanthine oxidase activity [74]. The consumption of chocolate powders and dark chocolates decreased UA crystallization through the increase in the amount of urinary theobromine [76]. Recent research indicated that theobromine, which is a dimethylxanthine that is abundant in cocoas and chocolates, can inhibit UA crystallization, suggesting it may be useful for the prevention of UA urolithiasis [77].

The 2012 American College of Rheumatology (ACR) Guidelines for Management of Gout [51] have recommended limiting intake of desserts in all gout patients.

## 6. Relationship Between the Number of Gout Patients and Beverage Consumption in Japanese People

### 6.1. Beverages

The daily beverage consumption of Japanese people in 2019 was higher compared to that in 2016 (2016: 605.1 g/day; 2019: 618.5 g/day). The daily beverage consumption of Japanese people was negatively correlated with the number of gout patients in 2004-2019 ( $r=-0.880$ ,  $p=0.0207$ ).

The daily beverage consumption of Japanese adult people (aged  $\geq 20$  years) and Japanese adult men (aged  $\geq 20$  years) in 2019 were higher compared to those in 2016, respectively [Japanese adult people (aged  $\geq 20$  years): 2016: 664.9 g/day; 2019: 673.5 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 740.6 g/day; 2019: 771.0 g/day]. Whereas the daily beverage consumption of Japanese adult women (aged  $\geq 20$  years) in 2019 was lower compared to that in 2016 (2016: 601.7 g/day; 2019: 588.4 g/day). In Japanese adult people (aged  $\geq 20$  years), Japanese adult men (aged  $\geq 20$  years), or Japanese adult women (aged  $\geq 20$  years), there was no significant correlation between the daily beverage consumption and the number of gout patients in 2004-2019 [Japanese adult people (aged  $\geq 20$  years):  $r=-0.667$ ,  $p=0.148$ ; Japanese adult men (aged  $\geq 20$  years):  $r=-0.514$ ,  $p=0.297$ ; Japanese adult women (aged  $\geq 20$  years):  $r=0.687$ ,  $p=0.131$ ]. This result suggests that the correlation of daily beverage consumption with the number of gout patients tends to vary with gender.

### 6.2. Sugar-Sweetened Beverages

The Ministry of Health, Labour and Welfare in Japan has not investigated the daily consumption of sugar-sweetened beverages of Japanese people.

Consumption of sugar-sweetened beverages, a major source of fructose, has risen sharply in recent decades all over the world [78]. The predominant sources of fructose in the diet are nonalcoholic beverages, which occupy 46% of total fructose intake [79].

In a randomized controlled trial, consumption of soft drinks (600 mL) increased plasma UA (PUA) concentrations by 17  $\mu\text{mol/L}$  at 60 min compared with the glucose control beverages (600 mL) [80]. A randomized controlled trial in overweight and obese subjects for 6 months showed that consumption of sucrose-sweetened soft drinks increased PUA concentrations compared with isocaloric milk, diet cola and water [81]. A pilot study in healthy, overweight women for 2 weeks revealed that the area under the curve (AUC) within 16 h (16h-AUC) for PUA concentrations was increased in subjects consuming sucrose-sweetened beverages compared with the baseline (before consuming sucrose-sweetened beverages) [82]. A pilot study in patients with chronic kidney disease, type 2 diabetes without chronic kidney disease, and in healthy subjects indicated that fructose drink (35 g fructose) increased postprandial serum uric acid (SUA) concentrations compared with the baseline (before consuming fructose drink) [83].

In epidemiological studies, increased intake of soft drinks was associated with increased SUA concentrations [25]. In epidemiological studies, increased intake of sugar-sweetened beverages was associated with increased SUA concentrations [27-30, 84-88], hyperuricemia risk [36, 84, 87, 89], and gout risk [28, 41, 43, 85, 89, 90]. The summarized results of the epidemiological studies of the association of sugar-sweetened beverages consumption with gout and hyperuricemia can be found in the meta-analysis prepared by Ebrahimpour-koujan et al. [89]. They [89] concluded that sugar-sweetened beverages consumption was significantly associated with increased risk of gout and hyperuricemia in adult population. Consumption of sugary beverages is low, because limiting intake of sugary beverages would reduce SUA levels [46]. Higher intake of high fructose corn syrup sources in products such as soft drinks can result in new onset of acute gout attacks [91]. These results suggest that limiting intake of sugar-sweetened beverages and soft drinks in Japanese people is essential for the prevention of gout.

The guidelines recommended the following for sugar-sweetened beverage intake: (1) limit intake of high fructose corn syrup-sweetened soft drinks and energy drinks, sweetened beverages, including serving of naturally sweet fruit juices and avoidance of high fructose corn syrup-sweetened sodas, other beverages, or foods for patients with gout [51]; (2) avoidance of intake of sugar-sweetened drinks for patients with gout [49]; avoidance of intake of sugar-sweetened drinks containing fructose for patients with gout [50].



### 6.3. Coffee and Tea

#### 1. Coffee

The daily intake of coffee and cocoa of Japanese people, Japanese adult people (aged  $\geq 20$  years), Japanese adult men (aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were higher compared to those in 2016, respectively [Japanese people: 2016: 133.3 g/day; 2019: 139.0 g/day; Japanese adult people (aged  $\geq 20$  years): 2016: 158.4 g/day; 2019: 164.0 g/day; Japanese adult men (aged  $\geq 20$  years): 2016: 163.0 g/day; 2019: 170.7 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 154.6 g/day; 2019: 158.1 g/day].

In epidemiological studies, increased intake of coffee was associated with decreased serum uric acid (SUA) concentrations [27, 92-94], hyperuricemia risk [32, 35, 43, 92, 93], and gout risk [35, 41-43, 95-100]. Coffee intake may prevent gout through a reduction of SUA concentrations and a decrease in hyperuricemia risk. As a possible mechanism of higher coffee intake associated with reduced gout risk, mediation analysis conducted by Hutton et al. [100] indicated that the urate-raising *GCKR* (rs1260326) and *ABCG2* (rs2231142) alleles were associated with both lower coffee intake and higher gout risk. They [100] have stated that these SNPs (single nucleotide polymorphisms) largely influences gout risk directly, rather than indirectly through effects on coffee intake.

#### 2. Tea

The daily intake of tea of Japanese people, Japanese adult people (aged  $\geq 20$  years), and Japanese adult women (aged  $\geq 20$  years) in 2019 were lower compared to those in 2016, respectively [Japanese people: 2016: 237.9 g/day; 2019: 237.1 g/day; Japanese adult people (aged  $\geq 20$  years): 2016: 267.1 g/day; 2019: 262.1 g/day; Japanese adult women (aged  $\geq 20$  years): 2016: 278.5 g/day; 2019: 269.7 g/day]. The daily intake of tea of Japanese adult men (aged  $\geq 20$  years) in 2019 was the same as that in 2016 (2016: 253.5 g/day; 2019: 253.5 g/day).

Intake of green tea [101] and black tea [102] decreased serum uric acid (SUA) concentrations. In epidemiological studies, increased intake of green tea was associated with increased SUA concentrations [103] but increased intake of tea drunk by Chinese adults was associated with decreased hyperuricemia risk [54, 104].

#### 3. Coffee and Tea

Coffee, green tea, and black tea contain caffeine (1, 3, 7-trimethyl xanthine). The amounts of caffeine contained in the leachate of coffee, green tea (gyokuro), green tea (sencha), and black tea were 60 mg/100mL, 160 mg/100mL, 20 mg/100mL, and 30 mg/100mL, respectively. In epidemiological studies, increased caffeine intake was associated with decreased serum uric acid (SUA) concentrations [41, 69, 105, 106]. Proposed mechanisms of higher coffee and tea intake associated with lower SUA levels and reduced hyperuricemia risk are presumed to involve the following three factors: (1) soluble dietary fiber suppresses the digestion and/or absorption of dietary purines in rats [107]; (2) caffeine may inhibit xanthine oxidase activity [108] and

enhance renal uric acid (UA) excretion [109]; (3) antioxidants, such as the phenol chlorogenic acid in coffee, the catechin in green tea, and the theaflavin in black tea may reduce SUA concentrations by inhibition of xanthine oxidase activity [110]. European Food Safety Authority (EFSA) [111] has recommended that the maximum daily intake of caffeine in healthy adults except pregnant women is 400 mg. It is imperative to drink coffee and/or tea, taking into account the daily caffeine intake.

The consumption of coffee in Japanese people in 2020 was 11.53 cups/week [112]. Poole et al. [98] have stated that the daily coffee consumption is three to four cups. The guidelines recommended encourage intake of coffee for patients with gout [50].

Since higher intake of coffee and tea decrease SUA concentrations and hyperuricemia risk, it seems that coffee and tea play an important role for the prevention of gout.

### 6.4. Alcoholic Beverages

The daily consumption of alcoholic beverages of Japanese people in 2019 was higher compared to that in 2016 (2016: 99.1 g/day; 2019: 106.6 g/day). The daily consumption of alcoholic beverages of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r=0.873$ ,  $p=0.000213$ ).

The daily consumption of beer of Japanese people in 2019 was higher compared to that in 2016 (2016: 62.0 g/day; 2019: 64.2 g/day). The daily consumption of beer of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r=0.702$ ,  $p=0.0109$ ).

The daily consumption of rice wine of Japanese people in 2019 was lower compared to that in 2016 (2016: 8.5 g/day; 2019: 7.2 g/day). The daily rice wine consumption of Japanese people was negatively correlated with the number of gout patients in 1986-2019 ( $r=-0.946$ ,  $p=0.00000329$ ).

The daily consumption of other liquors (e.g., foreign liquors) of Japanese people in 2019 was higher compared to that in 2016 (2016: 28.6 g/day; 2019: 35.2 g/day). The daily consumption of other liquors (e.g., foreign liquors) of Japanese people was positively correlated with the number of gout patients in 1986-2019 ( $r=0.974$ ,  $p=0.000000898$ ).

Alcoholic beverage consumption increased plasma uric acid (PUA) or serum uric acid (SUA) concentrations [113-116]. In epidemiological studies, increased consumption of alcoholic beverages was associated with increased SUA concentrations [25, 26, 31, 114, 115], hyperuricemia risk [34, 52], and gout risk [43, 115]. The above clinical research (clinical trials and epidemiological studies) showed that the degree of increase in SUA concentration, hyperuricemia risk, and gout risk varied according to the type of alcohol beverage. The daily consumption of alcoholic beverages was positively correlated with the number of gout patients in 2019 ( $r=0.873$ ,  $p=0.000213$ ). This result suggests that a decrease in daily consumption of alcoholic beverages in Japanese people is essential for the prevention of gout. Limiting or decreasing consumption of alcoholic beverages in Japanese people may play an important role in the prevention of gout through a

reduction of SUA concentrations and a decrease in hyperuricemia risk.

## 7. Conclusion

The number of patients with gout has been increasing in Japan [12]; that is to say, the number of gout patients of Japanese people in 2019 was higher compared to that in 2016 and increased 4.92-fold compared to that in 1986 (1986: 0.255 million; 2016: 1.105 million; 2019: 1.254 million) [12, 19]. The daily intake of total animal products, total meat, eggs, oils and fats, and alcoholic beverages of Japanese people in 2019 were higher compared to those in 2016, respectively. Whereas the daily intake of total seafood (fish and shellfish), milk and dairy products, seasonings, condiments and spices, and confectioneries of Japanese people in 2019 were lower compared to those in 2016, respectively. The significance of the correlation between the number of gout patients and intake of total meat, total seafood, eggs, seasonings, condiments and spices, oils and fats, confectioneries, or alcoholic beverages in 1986-2016 were also observed that in 1986-2019. Modification of intake of animal products, seasonings, condiments and spices, confectioneries, and beverages for the prevention of gout in Japanese people in 2019 is suggested as follows: limiting intake of meat; limiting alcohol beverage consumption; limiting or decreasing intake of salt, oils and fats, and confectioneries; avoidance of excessive intake of sugar-sweetened beverages and sugary foods including desserts and sweets; increasing the intake of milk and dairy products (particularly low-fat dairy products). Recognizing the intake of coffee and tea seems to be important for the prevention of gout in the general adult population. It is necessary to recognize and select what plant-based 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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