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Research Article

Modification of Macronutrient Intake for Prevention of Gout in Japanese People in 2022: 2024 Update

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Abstract

In Japan, the prevalence of gout has increased markedly since the 1960s. Following on from the previous report, the aim of this article is to suggest what macronutrient intake is important for the prevention of gout in Japanese people in 2022 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 (1986-2022) and the data of the National Health and Nutrition Survey in Japan (1946-2022) for the intake of macronutrients. Macronutrient intake of Japanese people in 2022 were compared with those in 2019. The relationship between the number of gout patients and macronutrient intake in Japanese people was examined. The number of gout patients of Japanese people in 2022 was higher compared to that in 2019 (2019: 1.254 million; 2022: 1.306 million). Almost all gout patients were adults, and the number of gout patients were higher in men than in women. Compared to the Japanese diet in 2019, in the Japanese diet in 2022, the mean ratio of energy intake from protein in total energy intake (Protein/Energy) was the same and the mean ratio of energy intake from fat in total energy intake (Fat/Energy) increased by 0.5% and the mean ratio of energy intake from carbohydrate in total energy intake (Carbohydrate /Energy) decreased by 0.5%. The daily intake of dietary fiber of Japanese men (aged ≥ 15 years) in 2022 was below the Adequate Intakes (AIs) established by the Institute of Medicine of the National Academy of Sciences in the U.S. The Fat/Energy and Saturated fatty acids/Energy and the daily intake of saturated fatty acids, monounsaturated fatty acids, and n-6 polyunsaturated fatty acids were positively correlated with the number of gout patients, respectively. Whereas the Protein/Energy and the daily intake of energy, total carbohydrate, total protein, animal protein, and vegetable protein were negatively correlated with the number of gout patients, respectively. Modification of macronutrient intake for the prevention of gout in Japanese people (especially adults) in 2022 is suggested as follows: 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, saturated fatty acids, cholesterol; increase intake of carbohydrate (particularly dietary fiber) and protein (particularly animal protein from low-fat dairy products and vegetable protein).

Keywords

Carbohydrate, Dietary Reference Intakes, Fat, Gout, Hyperuricemia, Protein, Saturated Fatty Acids, Uric Acid

1. Introduction

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 Gout Collaborators [1] estimates that the total number of individuals with gout in 2020 are 55.8 million people globally. Gout is the most common form of in-

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flammatory arthritis, and it is characterized by the deposition of monosodium urate (MSU) crystals that form in the presence of increased uric acid (UA) concentrations [2, 3]. The UA can promote metabolic inflammation and trigger the release of some key pro-inflammatory cytokines [4]. The clinical symptoms of gout develop in several stages, including asymptomatic hyperuricemia, MSU crystal formation, intermittent gout and chronic gout [5]. Pathophysiological stages of gout progression are as follows: (1) asymptomatic hyperuricemia; (2) acute gouty arthritis; (3) gout flares period; (4) chronic gouty arthritis with tophi [5]. The Japanese Society of Gout and Uric & Nucleic Acids [6] has recommended that serum uric acid (SUA) levels of patients with gout tophi should be kept below 6.0 mg/dL (356.9 μmol/L) for preventing recurrence of gouty arthritis. There is a strong association between serum uric acid (SUA) concentration and the risk of developing gout [7, 8], high body mass index (BMI) [9], older age [9], male sex [9], nationality [9]. A high SUA concentration (hyperuricemia) is frequently associated with gout [10]. Though hyperuricemia is a strong predictor of incident gout but not all patients with asymptomatic hyperuricemia will develop gout [11], management of SUA concentrations is important for the prevention and suppression of hyperuricemia and/or gout.

With lifestyle and dietary changes, the prevalence of hyperuricemia has gradually increased. The Japanese Society of Gout and Uric & Nucleic Acids [6] has stated that the number of patients with hyperuricemia has been increasing year by year as the diet becomes more Westernized in Japan and an increase in hyperuricemia and gout patients is attributed to changes in environmental factors (e.g., purine intake, fructose intake, meat and visceral intake, alcohol consumption, strenuous muscle exercise, stress, obesity) rather than genetic factors. The guidelines for the management of gout highlight the importance of limiting or avoiding the intake of purines [6], purine-rich foods (meat, seafood, organ meats, yeast extract) [10], sugar-sweetened drinks [11], desserts [10], table sugar [10], sauces and gravies [10], alcohol (especially beer and spirits) [6, 11], and heavy meals [11]. Furthermore, the guidelines have stated that important lifestyle changes in gout patients include weight control [6, 10, 11], physical activity [6, 10, 11], smoking cessation [10], and proper hydration [6, 10]. The prevalence of gout in Japan has increased markedly since the 1960s because of the westernization of the Japanese diet from 1955 [6, 12, 13]. For example, the introduction of the Western lifestyle to Japanese people, such as a diet containing greater amounts of meat and saturated fatty acids, has been associated with the increases in SUA levels and the incidence of hyperuricemia and gout [14]. At present, dietary recommendations have been updated worldwide. Diet can help to reduce the level of UA in the blood, alleviate gout symptoms, and prevent its recurrence through three major mechanisms: lowering UA production, increasing UA excretion, and reducing inflammation [15]. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 Gout Collaborators [1] estimates that the total number of individuals with gout will increase by more than 70% from 2020 to 2050, primarily due to population growth and ageing. Therefore, it is essential to implement dietary modification to prevent the future increase in gout patients in each region.

In Japan, the number of gout patients increased 0.149 million people from 2016 to 2019 (2016: 1.105 million; 2019: 1.254 million). It is important for the prevention of gout to assess the daily nutrient intake of Japanese people and to examine the relationship between the number of gout patients and the daily nutrient intake in Japanese people. The previous reports [16-19] showed modification of dietary habits for the prevention of gout in Japanese people through the trends in nutrient intakes of Japanese people in 1946-2019. Modification of macronutrient intake for the prevention of gout in Japanese people (especially adults) in 2019 is suggested as follows: 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; increase intake of carbohydrate (particularly dietary fiber).

Recently, the Ministry of Health, Labour and Welfare in Japan [22, 25] has shown the number of gout patients and the daily intake of nutrients or foods in 2022. Macronutrient intake of Japanese people in 2022 were compared with those in 2019. This article shows the relationship between the number of gout patients and macronutrient intake in Japanese people and suggests modification of macronutrient intake for the prevention of gout in Japanese people referencing the results of clinical research (clinical trials and epidemiological studies) through comparison with macronutrient intake in 2019 and 2022.

2. Methods

2.1. The Number of Gout Patients

The number of gout patients and serum uric acid (SUA) concentration was estimated in the Comprehensive Survey of Living Conditions performed by the Ministry of Health, Labour and Welfare in Japan (1986-2022) [13, 20-22]. 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 2022 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 (1946-2022) performed by the Ministry of Health, Labour and Welfare in Japan [23-25].

Data were extracted from the series of Japanese National Nutrition Surveys that have been carried out every year throughout Japan since 1946 [24]. 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 (1946-2022) [23, 25].

2.3. Dietary Reference Intakes for Japanese People

The Ministry of Health, Labour and Welfare in Japan [26] evaluates 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.

Dietary Reference Intakes definitions set by Institute of Medicine of the National Academy of Sciences in the U.S. [27] are as follows: (1) the Estimated Average Requirement (EAR) indicates the average daily nutrient intake level that is estimated to meet the requirements of half of the healthy individuals in a particular life stage and gender group; (2) the Recommended Dietary Allowance (RDA) indicates the average daily nutrient intake level that is sufficient to meet the nutrient requirements of nearly all (97-98 percent) healthy individuals in a particular life stage and gender group; (3) the Adequate Intake (AI) indicates the recommended average daily intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate; used when an RDA cannot be determined; and (4) the Tolerable Upper Intake Level (UL) indicates the highest average daily nutrient intake level that is likely to pose no risk of adverse health effects to almost all individuals in the general population. As intake increases above the UL, the potential risk of adverse effects may increase.

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 [28, 29] and the National Institutes of Health in the U.S. Department of Health & Human Services [30].

2.5. Statistical Analysis

The correlation efficient and the significance of the correlation between the number of gout patients and the mean daily nutrient intake in 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, 2019, and 2022 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. Results and Discussion

Table 1. *Trends in estimated number of gout patients in Japan in 2004-2022.*

Year	2004	2007	2010	2013	2016	2019	2022
Gender				million			
Total	0.874	0.854	0.957	1.063	1.105	1.254	1.306
Men	0.790	0.779	0.904	0.993	1.048	1.195	1.236
Women	0.083	0.074	0.053	0.069	0.057	0.059	0.070

Adapted from the Ministry of Health, Labour and Welfare in Japan [13, 20-22].

Table 2. *Trends in estimated number of gout patients by generations in Japan in 1998, 2016, 2019, and 2022.*

Year	**1998**	**2016**	**2019**	**2022**
Years old		**Thousand**		
Total				
15-24	2	4	3	1
25-34	15	17	19	22
35-44	68	84	83	79
45-54	124	180	206	211
55-64	159	270	296	315
65-74	152	340	393	415
75-84	61	173	216	214
≥ 85	9	35	38	48
Men				
15-24	2	4	2	1
25-34	14	16	19	20
35-44	67	81	82	78
45-54	116	177	204	207
55-64	137	261	288	302
65-74	125	326	373	396
75-84	43	155	199	192
≥ 85	6	27	28	39
Women				
15-24	0	0	0	0
25-34	1	1	0	2
35-44	1	1	0	1
45-54	8	4	1	4
55-64	22	9	9	12
65-74	27	14	20	19
75-84	18	19	17	21
≥ 85	3	8	10	9

Adapted from the Ministry of Health, Labour and Welfare in Japan [13, 20-22].

3.1. Prevalence of Gout in Japan

The number of gout patients going to hospitals estimated based on the Comprehensive Survey of Living Conditions conducted by the Ministry of Health, Labour and Welfare in Japan was 0.255 million in 1986, 0.283 million in 1989, 0.338 million in 1992, 0.423 million in 1995, 0.590 million in 1998, 0.696 million in 2001, 0.874 million in 2004, 0.854 million in 2007, 0.957 million in 2010, 1.063 million in 2013, 1.105 million in 2016, 1.254 million in 2019, and 1.306 million in 2022 [13, 20-22] (Table 1). These values clearly indicate a steady increase in the number of patients with gout in Japan.

The number of gout patients in Japanese adult population (aged ≥ 20 years) in 2022 was estimated to be 1.306 million [22]. The number of gout patients in Japanese adult men (aged ≥ 20 years) and Japanese adult women (aged ≥ 20 years) in

2022 were estimated to be 1.236 million and 0.070 million, respectively [22]. Almost all gout patients were adults, and the number of gout patients were higher in men than in women.

3.2. Relationship Between Prevalence of Gout and Age in Japan

The number of gout patients in Japanese people are shown in Table 2. The number of gout patients, especially men, increased with age in 1998-2022 [13, 20-22]. Japanese people who were 15-54 years old in 1998 increased gout patients after 2016. Compared to the number of total gout patients in Japanese people (aged 15-64 years) in 1998, the number of total gout patients in Japanese people (aged 35-84 years) in 2019 and 2022 markedly increased, approximately 20 years later [13, 20-22].

Compared to the number of total gout patients (aged ≥ 25 years) in 1998, the number of total gout patients (aged ≥ 25 years) in 2022 increased [13, 20-22]. Compared to the number of total gout patients (aged ≥ 45 years) in 2016 and 2019, the number of total gout patients (aged ≥ 45 years) in 2022 increased, except the number of total gout patients (aged 75-84 years) in 2019 [13, 20-22]. The number of total gout patients of Japanese people who are 45-74 years old and ≥ 85 years old in 2022 were higher than those in 1998, 2016, and 2019. Compared to the number of gout patients in men (aged ≥ 25 years) in 1998, 2016, and 2019, the number of gout patients in men (aged ≥ 25 years) in 2022 increased, except the number of gout patients in men (aged 35-44 years) in 2016 and 2019, and men (aged 75-84 years) in 2019 [13, 20-22]. Whereas compared to the number of gout patients in women (aged 45-74 years) in 1998, the number of gout patients in women (aged 45-74 years) in 2022 decreased [13, 20-22]. Compared to the number of gout patients (aged 25-34 years, ≥ 75 years) in 2016, the number of gout patients in women (aged 25-34 years, ≥ 75 years) in 2022 increased [13, 20-22]. Compared to the number of gout patients in women (aged ≥ 55 years) in 2016 and 2019, the number of gout patients in women (aged ≥ 55 years) in 2022 increased, except the number of gout patients in women (aged 65-74 years, ≥ 85 years) in 2019 [13, 20-22].

3.3. Relationship Between the Number of Gout Patients and Macronutrient Intake

The results on the correlation between the number of gout patients and macronutrient intake in Japanese people are shown in Tables 3 and 4. Since gout patients of Japanese people were aged 15 year or older in 1998-2022, this article evaluated the intake of nutrients in Japanese people aged 15 year or older.

Table 3. *Correlation between number of gout patients and macronutrient intake in Japanese people in 1986-2019 and 1986-2022.*

Year	**1986-2019**	**1986-2022**
Macronutrient	**coefficient**	**coefficient**
Energy	- 0.938***	- 0.919***
Total Carbohydrate	- 0.982***	- 0.985***
Dietary Fiber	- 0.214	0.033
Carbohydrate/Energy	- 0.358	- 0.519
Total Protein	- 0.887***	- 0.855***
Animal Protein	- 0.709*	- 0.612*
Vegetable Protein	- 0.960***	- 0.956***
Protein/Energy	- 0.661*	- 0.637*
Total Fat	- 0.210	0.055
Animal Fat	0.242	0.433
Vegetable Fat	- 0.676*	- 0.502
Fat/Energy	0.660*	0.737**
	2004-2019	2004-2022
	coefficient	coefficient
Cholesterol	0.294	0.614
	2007-2019	2007-2022
	coefficient	coefficient
SFAs	0.855	0.911*
SFAs/Energy	0.907*	0.943**
MUFAs	0.860	0.915*
n-3 PUFAs	- 0.098	- 0.132
n-6 PUFAs	0.776	0.867*

The Pearson Product Moment Correlation coefficient, * for P<0.05, ** for P<0.01, *** for P<0.001.

Abbreviation: Carbohydrate/Energy, Mean ratio of energy intake from carbohydrate in total energy intake; Protein/Energy, Mean ratio of energy intake from protein in total energy intake; Fat/Energy, Mean ratio of energy intake from fat in total energy intake; SFAs, Saturated fatty acids; SFAs/Energy, Mean ratio of energy intake from saturated fatty acids in total energy intake; MUFAs, monounsaturated fatty acids; n-3 PUFAs, n-3 polyunsaturated fatty acids; n-6 PUFAs, n-6 polyunsaturated fatty acids.

Table 4. *Correlation between number of gout patients and macronutrient intake in Japanese adult population, adult men, and adult women in 2004-2022.*

Year	Adults	Adult men	Adult women
2004-2022		coefficient	
Macronutrient			
Energy	0.0137	- 0.207	0.611
Total Carbohydrate	- 0.972***	- 0.971***	0.554
Dietary Fiber	0.831*	0.834*	- 0.129
Carbohydrate/Energy	- 0.967***	- 0.967***	0.316
Total Protein	0.356	0.268	0.537
Animal Protein	0.717	0.649	0.211
Vegetable Protein	- 0.616	- 0.864*	0.686
Protein/Energy	0.646	0.681	0.299
Total Fat	0.941**	0.944**	- 0.250
Animal Fat	0.949**	0.947**	- 0.259
Vegetable Fat	0.900**	0.917**	- 0.199
Fat/Energy	0.971***	0.975***	- 0.396
Cholesterol	0.703	0.651	0.100
2007-2022		coefficient	
SFAs	0.932**	0.927**	0.015
SFAs/Energy	0.943**	0.940**	- 0.029
MUFAs	0.929**	0.924**	0.004
n-3 PUFAs	- 0.132	- 0.220	0.065
n-6 PUFAs	0.893*	0.896*	0.022

The Pearson Product Moment Correlation coefficient, * for P<0.05, ** for P<0.01, *** for P<0.001.

Abbreviation: Carbohydrate/Energy, Mean ratio of energy intake from carbohydrate in total energy intake; Protein/Energy, Mean ratio of energy intake from protein in total energy intake; Fat/Energy, Mean ratio of energy intake from fat in total energy intake; SFAs, Saturated fatty acids; SFAs/Energy, Mean ratio of energy intake from saturated fatty acids in total energy intake; MUFAs, monounsaturated fatty acids; n-3 PUFAs, n-3 polyunsaturated fatty acids; n-6 PUFAs, n-6 polyunsaturated fatty acids.

3.3.1. Energy

The daily energy intake of Japanese people in 2022 was lower compared to that in 1960, 1965, 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, and 2019 and was higher compared to that in 2010, 2013, and 2016 (1960: 2096 kcal/day; 1965: 2184 kcal/day; 1975: 2188 kcal/day; 1986: 2075 kcal/day; 1989: 2061 kcal/day; 1992: 2058 kcal/day; 1995: 2042 kcal/day; 1998: 1979 kcal/day; 2001: 1954 kcal/day; 2004: 1902 kcal/day; 2007: 1898 kcal/day; 2010: 1849 kcal/day; 2013: 1873 kcal/day; 2016: 1865 kcal/day; 2019: 1903 kcal/day; 2022: 1888 kcal/day). The daily consumption of energy was negatively correlated with the number of gout patients in 1986-2019 (r= -0.938, p= 0.0000065) and in 1986-2022 (r= -0.919, p= 0.0000088).

The daily energy intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 1915 kcal/day; 2022: 1896 kcal/day). The daily consumption of energy did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.0133, p= 0.980) and in 2004-2022 (r= 0.0137, p= 0.977).

The daily energy intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 was lower compared to that in 2019, respectively (men: 2019: 2141 kcal/day; 2022: 2111 kcal/day, women: 2019: 1717 kcal/day; 2022: 1712 kcal/day). The daily consumption of energy did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.125, p= 0.814) and in 2004-2022 (r= -0.207, p= 0.656). The daily consumption of energy did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.599, p= 0.209) and in 2004-2022 (r= 0.611, p= 0.145).

The mean daily intake of energy for Japanese men (aged ≥ 20 years) and women (aged 20-59 years) in 2022 were 2064-2196 kcal/day and 1600-1720 kcal/day, respectively, and were below the estimation of energy requirement of low physical activity levels [physical activity levels: low: 2300 kcal/day; medium: 2650-2700 kcal/day; high: 3050 kcal/day among men; low: 1700-1750 kcal/day; medium: 2000-2050 kcal/day; high: 2300-2350 kcal/day among women] [26]. In Japanese men and women in 2022, the mean daily intake of energy for women (aged ≥ 60 years) was 1659-1763 kcal/day and was within the estimation of energy requirement of medium physical activity levels, and below the estimation of energy requirement of high physical activity levels [physical activity levels: low: 1400-1650 kcal/day; medium: 1650-2190 kcal/day; high: 2100-2250 kcal/day among women] [26]. The Institute of Medicine of the National Academy of Sciences in the U.S. has established the Estimate Energy Requirement (EER), which is defined as the average dietary energy intake that is predicted to maintain energy balance in a healthy adult of a defined age, gender, weight, height, and a level of physical activity that is consistent with good health [27].

A cross-sectional study using US National Health and Nutrition Examination Survey (NHANES) (2017-2018) data showed that dietary energy intake was positively correlated with SUA concentrations [31].

3.3.2. Carbohydrates

Carbohydrate

The daily carbohydrate intake of Japanese people in 2022 was lower compared to that in 1959, 1965, 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1959: 405 g/day; 1965: 384 g/day; 1975: 337 g/day; 1986: 295 g/day; 1989: 290 g/day; 1992: 289 g/day; 1995: 280 g/day; 1998: 271 g/day; 2001: 274 g/day; 2004: 266 g/day; 2007: 264 g/day; 2010: 258 g/day; 2013: 259 g/day; 2016: 252.8 g/day; 2019: 248.3 g/day; 2022: 244.8 g/day). The daily carbohydrate intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.982, p=0.0000000144) and in 1986-2022 (r= -0.985, p=0.000000000817).

The daily carbohydrate intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 248.7 g/day; 2022: 245.1 g/day). The daily carbohydrate intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.955, p=0.00301) and in 2004-2022 (r= -0.972, p= 0.000246).

The daily carbohydrate intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were lower compared to those in 2019, respectively (men: 2019: 275.3 g/day; 2022: 269.9 g/day, women: 2019: 225.5 g/day; 2022: 223.8 g/day). The daily carbohydrate intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.959, p= 0.00249) and in 2004-2022 (r= -0.971, p= 0.000270). The daily carbohydrate intake tended to be positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.788, p= 0.0624). The daily carbohydrate intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2022 (r= 0.554, p= 0.197). This result suggests that the correlation of daily carbohydrate intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The Ministry of Health, Labour and Welfare in Japan [26] has not set the Recommended Dietary Allowances (RDAs) for the daily carbohydrate intake in Japanese people. The Recommended Dietary Allowances (RDAs) for carbohydrates (sugars and starches) in the U.S. population (aged ≥ 1 year) established by the Institute of Medicine of the National Academy of Sciences in the U.S. is 130 g/day [27].

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that dietary carbohydrate intake was negatively correlated with SUA concentrations [31]. A cross-sectional study from China showed that every 10 g increase in energy-adjusted carbohydrate intakes caused a 5% decrease in hyperuricemia risk [32].

A large-scale prospective cohort study based on the UK Biobank involving 500,000 individuals (aged 40-69 years) in 2006-2010 found that total carbohydrates, total sugars, non-free sugars, total starch, refined grain starch, wholegrain starch, and fiber intake were associated with a reduced risk of gout, whereas free sugars intake were associated with an increased risk of gout [33]. This large-scale prospective cohort study found that total carbohydrates intake were associated with a reduced risk of gout; that is to say, individuals in the second level (230.50 - < 256.73 g/day), the third level (256.73 - < 281.42 g/day), the highest level (≥ 281.42 g/day) of the total carbohydrates intake were 21%, 31%, and 33% less likely to be gout compared to those individuals in the lowest intake level (< 230.50 g/day) (p for Trend = 3.073×10^{-15}) [33]. Hua et al. [33] revealed that SUA was identified as a significant mediator in all associations between total carbohydrates, total sugars, non-free sugars, total starch, refined grain starch, wholegrain starch, and fiber intake and gout risk. Detailed results are shown in the following sections.

Fructose

The Ministry of Health, Labour and Welfare in Japan has not investigated the daily fructose intake.

Previous reports [16, 18] showed the association between fructose intake and SUA concentrations, hyperuricemia risk or gout risk referencing the results of clinical research (clinical trials and epidemiological studies) reported. These results suggest that excessive intake of fructose and fructose-rich foods (e.g., high-fructose corn syrup and sugar-sweetened beverages, soft drinks) may lead to hyperuricemia and gout.

The results of a recently published article are presented below. Lecoultre et al. [34] found that fructose-induced hyperuricemia was associated with a decreased renal UA excretion in humans. Fang et al. [35] also reviewed the interaction between dietary fructose or fructose-rich diet and gut microbiota in hyperuricemia and gout. They [35] have stated that excessive fructose (especially in refined sugar and fruit juice) intake alters the gut microbiota composition and impairs intestinal barriers function through a series of inflammatory reactions, which play key roles in the pathogenesis of hyperuricemia and gout. A 10% fructose given intravenously (0.5 g/kg/h) for 2 hours increased blood lactate concentration, which may be attributable to decrease UA excretion via urate transporter 1 (URAT1/SLC22A12) [36]. Therefore, fructose intake has been shown to increase SUA level via both decreased UA excretion and increased UA production. In a systematic review and meta-analysis of controlled feeding trials, Wang et al. [37] have stated that high fructose intake (213-219 g/day) under hypercaloric feeding conditions (+35% excess energy) leads to increased risk of hyperuricemia and gout.

Anderson and Tulp [38] have stated that the recommended safe and healthful daily fructose intake is not entirely defined; however, 25-50 grams a day is often indicated as safe, with 50-100 grams a day as being high, and over 100 grams a day as potentially dangerous for human consumption.

The Japanese Society of Gout and Uric & Nucleic Acids Guidelines [6] has recommended avoidance of fructose overdose in patients of gout. The 2020 American College of

Rheumatology (ACR) Guideline [39] has conditionally recommended for limiting high-fructose for patients with gout, regardless of disease activity.

Foods high in fructose are as follows: raisins, date palm, dried figs, dried mango, dried tomatoes, dried kanpyo, dried apricots, dried prunes, ginger powder, grape, apple, dried banana, lychee, cherimoya, pear, cherry, kiwifruit, quince, gooseberry, persimmon, fig, mango, blueberry [28].

Anderson and Tulp [38] have stated that fructose as a limited normal constituent of fruits and vegetables has always likely been a minor constituent of the human diet, where it occurs in combination with dietary fibers, gums and other dietary components that collectively slow its rate of luminal absorption and postprandial disposal.

Sugars

Sugars from diets can be absorbed as glucose, galactose or fructose in the liver portal circulation. The liver and gut normally process galactose and fructose into lactate, glucose and organic acids through gluconeogenesis, glycogenolysis, aerobic oxidation and other pathway [40]. Metabolism of glucose, fructose or galactose is reviewed in detail by Chandel [40].

The World Health Organization (WHO) has stated that the term “sugars” includes intrinsic sugars, which are those incorporated within the structure of intact fruit and vegetables; sugars from milk (lactose and galactose); and free sugars, which are monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook or consumer, and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrates [41].

The Ministry of Health, Labour and Welfare in Japan has not investigated the daily intake of sucrose, glucose and fructose. The Ministry of Health, Labour and Welfare in Japan [26] has not set the Recommended Dietary Allowances (RDAs) for the daily intake of sugars (monosaccharides, disaccharides, sugar alcohols) in Japanese people.

Considering the results of clinical research (clinical trials and epidemiological studies) reported, the previous reports [16, 18] suggest excessive intake of sugars (particularly fructose and sucrose) may lead to hyperuricemia and gout. The detailed results of these articles have been described in the previous article [16, 18].

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that no statistical difference was found about the associations of dietary total sugars intake with SUA concentrations [31]. In Mendelian randomization analysis, higher intake of sugar was associated with increased SUA levels [42]. An isocaloric sucrose diet in gouty patients increased SUA concentrations [43].

A large-scale prospective cohort study found that free sugars intake were associated with an increased risk of gout; that is to say, individuals in the second level (42.44 -< 5 7.73 g/day), the highest level (≥ 75.61 g/day) of the free sugars intake were 1% and 15% more likely to be gout compared to those individuals in the lowest intake level (< 42.44 g/day), respectively and individuals in the third level (57.73 - < 75.61 g/day) of the free sugars intake was 1% less likely to be gout compared to those individuals in the lowest intake level (< 42.44 g/day) (p for Trend = 0.014) [33]. Whereas total sugars and non-free sugars intake were associated with a reduced risk of gout; that is to say, individuals in the second level (100.97 - < 122.91 g/day), the third level (122.91 - < 146.72 g/day), the highest level (≥ 146.72 g/day) of the total sugars intake were 16%, 18%, and 11% less likely to be gout compared to those individuals in the lowest intake level (< 100.97 g/day) (p for Trend = 0.018) [33]. Furthermore, non-free sugars intake were associated with a reduced risk of gout; that is to say, individuals in the second level (43.88 - < 60.70 g/day), the third level (60.70 - < 80.04 g/day), the highest level (≥ 80.04 g/day) of the non-free sugars intake were 22%, 28%, and 30% less likely to be gout compared to those individuals in the lowest intake level (< 43.88 g/day) (p for Trend = 2.100×10^{-11}) [33].

Tappy et al. [44] have proposed to set a maximum limit to the intake of total sugars containing fructose (sucrose, glucose fructose syrups, honey or other syrups, and natural concentrates, etc.) of 100 g/day. Recommendation for added sugars naturally present in established by the Institute of Medicine of the National Academy of Sciences in the U.S. suggests limit to a maximal intake of no more than 25 percent total energy [27]. The World Health Organization (WHO) recommends reducing the intake of free sugars to less than 10% of total energy intake in both adults and children and suggests a further reduction of the intake of free sugars to below 5% of total energy intake [41]. The 2015-2020 Edition of the Dietary Guidelines for Americans [45] recommends consuming less than 10% calories per day from added sugar and does not include sugars fruit juices added sugars. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of free sugars is < 10% of energy.

The 2012 American College of Rheumatology (ACR) Guidelines for Management of Gout [10] has recommended limiting intake of table sugar in all gout patients. The Italian Society of Rheumatology clinical practice guidelines for the diagnosis and management of gout [47] has recommended low in added sugars.

As described in the previous articles [16, 18], it should pay attention to not to excessive intake of sugars (particularly fructose and sucrose) to prevent hyperuricemia and/or gout.

Starches

The Ministry of Health, Labour and Welfare in Japan has not investigated the daily starch intake.

A large-scale prospective cohort study based on the UK Biobank involving 500,000 individuals (aged 40-69 years) in 2006-2010 found that total starch, refined grain starch, wholegrain starch intake were associated with a reduced risk of gout; that is to say, individuals in the second level (109.29 - < 129.26 g/day), the third level (129.26 - < 149.44 g/day), the highest level (≥ 149.44 g/day) of the total starch intake were 19%, 28%, and 30% less likely to be gout compared to those individuals in the lowest intake level (< 109.29 g/day) (p for Trend = 7.254 $\times 10^{-12}$) [33]. Refined grain starch intake were associated with a reduced risk of gout; that is to say, individuals in the second level (96.21 - < 153.17 g/day), the third level (153.17 - < 222.30 g/day), the highest level (≥ 222.30 g/day) of the refined grain starch intake were 9%, 12%, and 15% less likely to be gout compared to those individuals in the lowest intake level (< 96.21 g/day) (p for Trend = 0.002) [33]. Furthermore, wholegrain starch intake were associated with a reduced risk of gout; that is to say, individuals in the second level (45.99 - < 96.03 g/day), the third level (96.03 - < 162.67 g/day), the highest level (≥ 162.67 g/day) of the wholegrain starch intake were 5%, 19%, and 27% less likely to be gout compared to those individuals in the lowest intake level (< 45.99 g/day) (p for Trend = 1.536 $\times 10^{-9}$) [33].

Dietary Fiber

The daily intake of dietary fiber of Japanese people in 2022 was lower compared to that in 1951, 1955, 1960, 1975, and 2019 and was higher compared to that in 1986, 1989, 1992, 1998, 2001, 2004, 2007, 2010, 2013, and 2016 and was the same as that in 1966 (1951: 23.3 g/day; 1955: 23.0 g/day; 1960: 19.9 g/day; 1966: 18.1 g/day; 1975: 18.3 g/day; 1986: 16.6 g/day; 1989: 16.4 g/day; 1992: 16.4 g/day; 1998: 15.0 g/day; 2001: 14.6 g/day; 2004: 13.9 g/day; 2007: 14.6 g/day; 2010: 14.0 g/day; 2013: 14.2 g/day; 2016: 14.2 g/day; 2019: 18.4 g/day; 2022: 18.1 g/day). The daily dietary fiber intake did not show a significant correlation with the number of gout patients in 1986-2019 (r= -0.214, p= 0.476) and in 1986-2022 (r= 0.033, p= 0.918).

The daily intake of dietary fiber of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 18.8 g/day; 2022: 18.5 g/day). The daily intake of dietary fiber did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.730, p= 0.0994). Whereas the daily dietary fiber intake was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022 (r= 0.831, p= 0.0206).

The daily dietary fiber intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were lower compared to that in 2019, respectively (men: 2019: 19.9 g/day; 2022: 19.5 g/day, women: 2019: 18.0 g/day; 2022: 17.6 g/day). The daily intake of dietary fiber did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.742, p= 0.0913). Whereas the daily dietary fiber intake was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= 0.834, p= 0.0198). The daily intake of dietary fiber did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.270, p= 0.605) and in 2004-2022 (r= -0.129, p= 0.782). This result suggests that the correlation of the daily intake of dietary fiber with the number of gout patients varies with gender.

The daily intake of dietary fiber of Japanese men (aged ≥ 15 years) in 2022 was about the same as that in 2019 (2019: 17.5-21.4 g/day; 2022: 17.6-21.5 g/day). The daily intake of dietary fiber of Japanese women (aged ≥ 15 years) in 2022 was about the same as that in 2019 (2019: 14.6-19.8 g/day; 2022: 13.7-20.1 g/day). The daily dietary fiber intake of Japanese men (aged 20-59 years) and women (aged 20-59 years) in 2022 were 17.6-18.9 g/day (8.37-8.90 g/1000kcal) and 13.7-16.9 g/day (8.56-9.83 g/1000kcal), respectively, and were below the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan [men (aged 18-64 years): ≥ 21 g/day; women (aged 15-64 years): ≥ 18 g/day] [26]. The daily dietary fiber intake of Japanese men (aged ≥ 70 years) and women (aged ≥ 60 years) were 21.5 g/day (10.86 g/1000kcal) and 18.6-20.1 g/day (10.55-11.40 g/1000kcal), respectively, and were above the DG established by the Ministry of Health, Labour and Welfare in Japan [men (aged ≥ 65 years): ≥ 20 g/day; women (aged 15-64 years): ≥ 18 g/day; women (aged ≥ 65 years): ≥ 17 g/day] [26]. The U.S. Department of Agriculture (USDA) has recommended that daily dietary fiber intake is 14 g/1000kcal, for an average age adult, this means a daily intake of 25 g (female) or 38 g (male) in the U.S. [45]. Recommended Adequate Intakes (AIs) for total fiber (the sum of dietary fiber and functional fiber) in the U.S. population (aged ≥ 1 year) established by the Institute of Medicine of the National Academy of Sciences in the U.S. is 14 g/1,000 kcal [men (aged 14-50 years): 38 g/day; men (aged ≥ 51 years): 30 g/day; women (aged 9-18 years): 26 g/day; women (aged 19-50 years): 25 g/day; women (aged ≥ 51 years): 21 g/day] [27]. The daily intake of dietary fiber of Japanese men (aged ≥ 15 years) in 2022 was below the AIs established by the Institute of Medicine of the National Academy of Sciences in the U.S. [27]. The Nordic Nutrition Recommendations 2012 [48] has stated that the recommended intake of dietary fiber is 35 g/d for men and 25 g/d for women and dietary fiber is beneficial for health, advocating intakes of at least 25 g/day. Results of the German National Nutrition Monitoring (NEMONIT) [49] have shown that adults are recommended to consume over 30 g/day of fiber. The European Food Safety Authority [50] has recommended 25 g as the sufficient fiber consumption in adults. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of dietary fiber is > 25 g/day for adults for preventing obesity, diabetes, cardiovascular diseases and various cancers. Therefore, the daily dietary fiber intake for Japanese adult men and women (aged ≥ 20 years) were below the recommendation by the U.S. Department of Agriculture (USDA) [45], the Nordic Nutrition Recommendations 2012 [48], the German National Nutrition Monitoring (NEMONIT) [49], The European Food Safety Authority [50], and The Joint WHO/FAO Expert Consultation [46].

In epidemiological studies, increased dietary fiber intake was associated with decreased SUA concentrations [31, 51-56], hyperuricemia risk [32, 51-53, 55-58], and gout risk [33, 59]. In a clinical trial, dietary fiber decreased serum uric acid (SUA) concentrations [60, 61]. The previous article [18] showed that the detailed results of effect of dietary fiber on SUA concentrations and hyperuricemia risk [51-53, 55, 58, 60, 61]. Dietary fiber intake may prevent gout through reduced SUA concentrations and decreased hyperuricemia risk. The previous articles [18, 62] describe a possible mechanism for the suppression of elevation of SUA concentrations of fiber ingested in experimental hyperuricemia model in animal species. It seems that increase intake of carbohydrate (particularly dietary fiber) may play an important role for the prevention of gout.

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that dietary fiber intake was negatively correlated with SUA concentrations [31]. A cross-sectional study from China showed that every 10 g increase in energy-adjusted dietary fiber intakes caused a 13% decrease in hyperuricemia risk [32]. A cross-sectional study survey using the seventh Korean National Health and Nutrition Examination Survey 2016-2018 data collected for 15278 subjects (6455 men and 8823 women) (aged ≥ 20 years) showed that dietary fiber intake was inversely associated with SUA concentrations in both men and women [56]. Consuming more than 27.9 g of dietary fiber in men and 20.7 g in women reduced hyperuricemia risk by 28% and 29% in men and women, respectively [hyperuricemia: SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women]. Men in the highest quartile of intake of total dietary fiber, cereal fiber, vegetable fiber, and fruit fiber were 38.9%, 29.7%, 23.9%, and 28.4% less likely to be hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men] compared to those subjects in the lowest quartile of each fiber intake, respectively [56]. Women in the highest quartile of intake of total dietary fiber, cereal fiber, vegetable fiber, and fruit fiber were 34.7%, 27.9%, 27.5%, and 20.2% less likely to be hyperuricemia [SUA concentration ≥ 6.0 mg/dL (356.9 μmol/L) in women] compared to those subjects in the lowest quartile of each fiber intake, respectively [56].

Dietary glycemic load values, which reflect both quality and quantity of dietary carbohydrate intake, were negatively correlated with total fiber intake in Chinese adults in the China Health and Nutrition Survey 2009 [63]. Higher dietary glycemic load values, which reflect both quality and quantity of dietary carbohydrate intake, were significantly associated with an increased prevalence of hyperuricemia in Chinese adults in the China Health and Nutrition Survey 2009 [63]. These results suggest that an increased hyperuricemia risk may be partially due to the low intake of dietary fiber.

The exact mechanism for the beneficial effect of dietary fiber intake on gout remains largely unknown.

In an experimental model of gout in mice, which are made by injection of monosodium urate crystals into the knee joint, a high-fiber diet (5% cellulose + 10% pectin) controlled the inflammatory response to monosodium urate crystals by favoring the resolution of the inflammatory response [64]. In the same mouse model of gout, a pectin-rich fiber diet increased serum acetate concentrations and showed reduced joint destruction and decreased joint dysfunction (hypernociception) and interleukin-1β (IL-1β) production, compared with the cellulose diet [64]. Therefore, high intake of dietary fiber had a positive effect on the resolution of a gout flare in an experimental model of mice with gout [64]. High-fiber diet alleviated the inflammatory response induced by monosodium urate crystals through short chain fatty acids (SCFAs) production [64].

Cao and Hu [65] used the interpretable machine learning model based on SHapley Additive exPlanations (SHAP) to assess the contribution of dietary fiber in predicting gout using datasets from the NHANES (2005-2018). In the interpretable Light Gradient Boosting Machine (LGBM) model, increasing dietary fiber intake reduced the potential risk of gout. A large-scale prospective cohort study found that fiber intake was associated with a reduced risk of gout; that is to say, individuals in the second level (14.23 - < 17.43 g/day), the third level (17.43 - < 20.98 g/day), the highest level (≥ 20.98 g/day) of the fiber intake were 26%, 24%, and 28% less likely to be gout compared to those individuals in the lowest intake level (< 14.23 g/day) (p for Trend = 2.638×10^{-9}) [33].

Judging from the data of food composition [28, 30, 66], it is important for Japanese people to eat seeds and nuts (pumpkin seeds, chia seeds, almonds, chestnuts, sunflower seeds, pine nuts, pistachio nuts, hazelnuts, peanuts, coconut), whole grains (high fiber-bran ready-to-eat cereals, shredded wheat ready-to-eat cereals, popcorn, bulgur, spelt, whole grain bread, oats, barley, rye), legumes (lima beans, navy beans, small white beans, yellow beans, green peas, adzuki beans, cranberry beans, adzuki beans, French beans, split peas, chickpeas, lentils, pinto beans), seaweed, mushrooms (wood ear, shiitake mushrooms, maitake mushrooms), potatoes (sweet potato, konjac, potato with skin), fruit (sapote or sapodilla, guava, nance, avocados, apples, raspberries, loganberries, blackberries, pear, kiwifruit, grapefruit, apple with skin, prunes, oranges, bananas,), and vegetables (artichokes, pumpkins, taro root (dasheen or yautia), brussels sprouts, tomatoes, broccoli, carrots, sweet corn, pears) to take in more dietary fiber to reach the DG established by the Ministry of Health, Labour and Welfare in Japan and recommended AIs established by the U.S. Department of Agriculture (USDA), the recommended intake by the Nordic Nutrition Recommendations 2012 [48], and the German National Nutrition Monitoring (NEMONIT) [49], the European Food Safety Authority [50], and the Joint WHO/FAO Expert Consultation [46]. Though the daily dietary fiber intake was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022, it seems that Japanese adult population (aged ≥ 20 years) need to take in more dietary fiber. Increase in intake of fiber-rich foods (e.g., whole grains, legumes, seeds and nuts, fruit, vegetables) in Japanese people seems to be important for the prevention of gout.

Other article will describe the importance of intake of dietary fiber for the prevention of hyperuricemia and/or gout in Japanese people in detail including the role of dietary fiber on gut microbiota.

Ratio of Energy Intake from Carbohydrate in Total Energy Intake

The mean ratio of energy intake from carbohydrate in total energy intake (Carbohydrate/Energy) of Japanese people in 2022 was lower compared to that in 1975, 1980, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1975: 63.1%; 1980: 61.5%; 1986: 60.3%; 1989: 58.7%; 1992: 58.9%; 1995: 57.8%; 1998: 57.8%; 2001: 59.7%; 2004: 59.7%; 2007: 59.3%; 2010: 59.4%; 2013: 58.9%; 2016: 57.8%; 2019: 56.3%; 2022: 55.8%). The Carbohydrate/Energy did not show a significant correlation with the number of gout patients in 1986-2019 (r= -0.358, p= 0.253) and in 1986-2022 (r= -0.519, p= 0.0690).

The Carbohydrate/Energy of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 56.4%; 2022: 55.9%). The Carbohydrate/Energy was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.932, p= 0.00687) and in 2004-2022 (r= -0.967, p= 0.000377).

The Carbohydrate/Energy of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were lower compared to those in 2019, respectively (men: 2019: 57.8%; 2022: 57.0%, women: 2019: 55.3%; 2022: 54.9%). The Carbohydrate/Energy was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.954, p=0.00314) and in 2004-2022 (r= -0.967, p= 0.000383). The Carbohydrate/Energy did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.541, p= 0.268) and in 2004-2022 (r= 0.316, p= 0.490). This result suggests that the correlation of the Carbohydrate/Energy with the number of gout patients varies with gender.

The results of a recently published article are presented below. In a cross-sectional study in 7886 Chinese adults who participated in the China Health and Nutrition Survey 2009, substituting 5% of energy intake from the total protein for carbohydrates was associated with increase in SUA concentrations [67].

The Carbohydrate/Energy of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 55.1-59.2% of energy and 52.3-58.2% of energy, respectively, and were within the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan [men (aged ≥ 1 year): 50-65% of energy; women (aged ≥ 1 year): 50-65% of energy] [26] or the Acceptable Macronutrient Distribution Ranges (AMDRs) set by the Institute of Medicine of the National Academy of Sciences in the U.S. [27]. The Institute of Medicine of the National Academy of Sciences in the U.S. has determined that the AMDRs, which is defined as a range of intakes for a particular energy source that is associated with reduced risk of chronic disease while providing adequate intakes of essential nutrients, for carbohydrates both adults (aged ≥ 19 years) and children (aged 1-18 years) is 45-65 percent of total calories [27]. Furthermore, the Joint WHO/FAO Expert Consultation [46] has stated that the recommended the Carbohydrate/Energy is 15-75% of total energy (calories). Intake of fiber-rich foods (e.g., whole grains, legumes, seeds and nuts, fruit, vegetables) seems to be important for the prevention of gout.

3.3.3. Proteins

Total Protein

The daily total protein intake of Japanese people in 2022 was lower compared to that in 1975, 1986, 1989, 1992, 1995, 1998, 2001, and 2019 and was higher compared to that in 1960, 2004, 2007, 2010, 2013, and 2016 and was the same as that in 1965 (1960: 69.7 g/day; 1965: 71.3 g/day; 1975: 80.0 g/day; 1986: 78.9 g/day; 1989: 80.2 g/day; 1992: 80.1 g/day; 1995: 81.5 g/day; 1998: 79.2 g/day; 2001: 73.4 g/day; 2004: 70.8 g/day; 2007: 69.8 g/day; 2010: 67.3 g/day; 2013: 68.9 g/day; 2016: 68.5 g/day; 2019: 71.4 g/day; 2022: 71.3 g/day). The daily total protein intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.887, p= 0.000118) and in 1986-2022 (r= -0.855, p= 0.000197).

The daily total protein intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 72.2 g/day; 2022: 71.9 g/day). The daily intake of total protein did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.159, p= 0.764), and in 2004-2022 (r= 0.356, p= 0.433).

The daily total protein intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were lower compared to those in 2019, respectively (men: 2019: 78.8 g/day; 2022: 78.5 g/day, women: 2019: 66.4 g/day; 2022: 66.2 g/day). The daily intake of total protein did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.077, p= 0.885) and in 2004-2022 (r= 0.268, p= 0.561). The daily intake of total protein did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.527, p= 0.283) and in 2004-2022 (r= 0.537, p= 0.214).

The mean daily total protein intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 76.5-90.8 g/day and 60.2-70.4 g/day, respectively, and exceeded the recommended dietary allowances (RDAs) [men (aged ≥ 15 years): 60-65 g/day; women (aged ≥ 15 years): 50-55 g/day] [26]. The RDAs for protein in the U.S. adults (aged ≥ 19 years) established by the Institutes of Medicine is 0.8 g/kg body weight for the reference body weight [27, 68]. In healthy adult men and women, protein intake should not exceed the World Health Organization (WHO) recommendation (0.83 g/ kg body weight/day for adults [69]). UK Gout Society [70] has stated that gout patients need about 1 g of protein per kg of body weight, unless they on a protein restricted diet (e.g., some people with kidney disease may need to restrict protein intake). The Ministry of Health, Labour and Welfare in Japan [26] has not set a Tolerable Upper Intake Levels (ULs) for healthy individuals because there are insufficient reports of clear scientific evidence for health problems due to excessive daily intake of protein. However, excessive intake of protein can reduce renal function. A meta-analysis concluded that higher protein intake (≥ 20% but < 35% of energy or ≥ 10% higher than a comparison intake) within the range of recommended intakes for protein was consistent with normal renal function in healthy individuals in the short term (and did not reduce renal function) [71]. In healthy adults, consuming a higher-protein diet did not cause changes in kidney function compared with lower- or normal-protein diets [72].

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that no statistical difference was found about the associations of dietary protein intake with SUA concentrations [31]. A cross-sectional study from China showed that every 10 g increase in energy-adjusted protein intakes caused a 17% increase in hyperuricemia risk [32]. In a 6-year follow-up study of 1621 community-dwelling Chinese participants (aged 50-70 years) without hyperuricemia [SUA concentration > 420.0 μmol/L in men and > 360.0 μmol/L in women], plasma cysteine, glutamine, phenylalanine, threonine, and long-chain acylcarnitines were positively associated with incident hyperuricemia [73]. Wang et al. [73] have stated that the levels of these metabolites may be partially driven by intakes of meat and soy products that are associated with hyperuricemia.

In a prospective cohort study in a Chinese population, higher intake of total protein, protein from poultry, protein from seafood (fish and shellfish) was associated with increased gout risk, respectively, whereas higher intake of protein from soy foods and protein from nonsoy legumes was associated with decreased gout risk, respectively [74]. Protein intake from red meat, eggs, dairy products, grain products, or nuts and seeds had no association with gout risk, respectively [74].

Animal Protein

The daily animal protein intake of Japanese people in 2022 was higher compared to that in 1960 1965, 1975, 1986, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 and was lower compared to that in 1989, 1992, 1995, and 1998 (1960: 24.7 g/day; 1965: 28.5 g/day; 1975: 38.9 g/day; 1986: 40.1 g/day; 1989: 42.4 g/day; 1992: 42.5 g/day; 1995: 44.4 g/day; 1998: 42.8 g/day; 2001: 39.9 g/day; 2004: 38.0 g/day; 2007: 38.0 g/day; 2010: 36.0 g/day; 2013: 37.2 g/day; 2016: 37.4 g/day; 2019: 40.1 g/day; 2022: 40.4 g/day). The daily intake of animal protein was negatively correlated with the number of gout patients in 1986-2019 (r= -0.709, p= 0.00985) and in 1986-2022 (r= -0.612, p= 0.0262).

The daily animal protein intake of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 40.1 g/day; 2022: 40.4 g/day). The daily intake of animal protein did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.541, p= 0.267) and in 2004-2022 (r= 0.717, p= 0.0698).

The daily animal protein intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 44.3 g/day; 2022: 44.6 g/day, women: 2019: 36.4 g/day; 2022: 36.7 g/day). The daily intake of animal protein did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.451, p= 0.369) and in 2004-2022 (r= 0.649, p= 0.115). The daily intake of animal protein did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.154, p= 0.771) and in 2004-2022 (r= 0.211, p= 0.649).

The results of a recently published article are presented below. A cross-sectional study from China showed that every 10 g increase in energy-adjusted animal protein intakes caused a 18% increase in hyperuricemia risk [32]. In a cross-sectional study in 7886 Chinese adults who participated in the China Health and Nutrition Survey 2009, dietary animal protein (red meat 48.8%; egg 24.7%; fish and seafood 15.5%; white meat 7.7%; offal 1.8%; dairy 1.5%) intake was associated with increased SUA concentrations [67]. The potential underlying mechanisms of the positive associations between animal protein intake and SUA levels may be attributable to the effects of amino acids on purine synthesis and/or the exogenous purine from foods enriched in animal protein [75]. In a 3-phase randomized, crossover metabolic study in healthy subjects (aged 18-70 years), consuming animal protein was associated with increased SUA concentrations and amount of urinary UA excretion [76].

In a clinical trial, animal sources of protein (e.g., casein, lactalbumin [77, 78]) decreased SUA concentrations. Ingestion of milk (casein and lactalbumin) has been shown to decrease SUA levels in healthy subjects via the uricosuric effect of these proteins [78]. An increase in intake of milk (particularly a low-fat milk) and cheese seems to be important for the prevention of gout through a decrease in SUA concentrations.

Vegetable Protein

The vegetable protein is from grains, potatoes, legumes, seeds, nuts, fruit, vegetables, mushrooms, and seaweed. The daily vegetable protein intake of Japanese people in 2022 was lower compared to that in 1960, 1965, 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1960: 45.0 g/day; 1965: 42.8 g/day; 1975: 41.1 g/day; 1986: 38.8 g/day; 1989: 37.8 g/day; 1992: 37.6 g/day; 1995: 37.1 g/day; 1998: 36.4 g/day; 2001: 33.5 g/day; 2004: 32.8 g/day;

2007: 31.8 g/day; 2010: 31.3 g/day; 2013: 31.7 g/day; 2016: 31.1 g/day; 2019: 31.3 g/day; 2022: 30.9 g/day). The daily vegetable protein intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.960, p= 0.000000715) and in 1986-2022 (r= -0.956, p= 0.000000330).

The daily vegetable protein intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 32.1 g/day; 2022: 31.5 g/day). The daily intake of vegetable protein did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.507, p= 0.304) and in 2004-2022 (r= -0.616, p= 0.141).

The daily vegetable protein intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were lower compared to those in 2019, respectively (men: 2019: 34.5 g/day; 2022: 33.9 g/day, women: 2019: 30.0 g/day; 2022: 29.5 g/day). The daily intake of vegetable protein tended to be negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.788, p= 0.0628). The daily intake of vegetable protein was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= -0.864, p= 0.0121). The daily intake of vegetable protein was positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.865, p= 0.0262). The daily intake of vegetable protein did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2022 (r= 0.686, p= 0.0887). This result suggests that the correlation of daily vegetable protein intake with the number of gout patients tends to vary with gender.

The results of a recently published article are presented below. In a cross-sectional study in 7886 Chinese adults who participated in the China Health and Nutrition Survey 2009, dietary plant protein (grains 68.9%; legumes 13.8%; fruits and vegetables 13.1%; tubers 2.0%; nuts 1.4%; fungi and algae 0.7%) intake was associated with decreased SUA concentrations in the unadjusted models, while that was not significantly associated with SUA concentrations in the fully-adjusted models [67]. A cross-sectional study from China showed that every 10 g increase in energy-adjusted plant-derived protein intakes caused a 10% decrease in hyperuricemia risk [32].

Vegetable sources of protein (e.g., wheat gluten [79], rice endosperm protein [80]) decreased SUA concentrations. An increase in intake of wheat gluten and rice endosperm protein seems to be important for the prevention of gout through a decrease in SUA concentrations. Intake of casein, lactalbumin, wheat gluten, and rice endosperm protein seem to be important for the prevention of gout through a decrease in SUA concentrations.

Ratio of Energy Intake from Protein in Total Energy Intake

The mean ratio of energy intake from protein in total energy intake (Protein/Energy) of Japanese people in 2022 was higher compared to that in 1975, 1980, 2007, 2010, 2013, and 2016 was lower compared to that in 1986, 1989, 1992, 1995, and 1998 and was about the same as that in 2002, 2005, and 2019 (1975: 14.6%; 1980: 14.9%; 1986: 15.2%; 1989: 15.6%; 1992: 15.6%; 1995: 16.1%; 1998: 16.1%; 2002: 15.1%; 2005: 15.1%; 2007: 14.8%; 2010: 14.7%; 2013: 14.8%; 2016: 14.8%; 2019: 15.1%; 2022: 15.1%). The Protein/Energy was negatively correlated with the number of gout patients i in 1986-2019 (r= -0.661, p= 0.0192) and in 1986-2022 (r= -0.637, p= 0.0193).

The Protein/Energy of Japanese adult population (aged ≥ 20 years) in 2022 was the same as that in 2019 (2019: 15.2% of energy; 2022: 15.2% of energy). The Protein/Energy did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.458, p= 0.361) and in 2004-2022 (r= 0.646, p= 0.117).

The Protein/Energy of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 14.8% of energy; 2022: 14.9% of energy, women: 2019, 15.5% of energy; 2022: 15.6% of energy). The Protein/Energy did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.470, p= 0.347) and in 2004-2022 (r= 0.681, p= 0.092). The Protein/Energy did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.275, p=0.598) and in 2004-2022 (r= 0.299, p= 0.514).

The Protein/Energy of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 14.7-15.1% of energy and 14.7-16.0% of energy, respectively, and were within the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan [men (≥ 15 year): 13-20% of energy; women (aged ≥ 15 year): 13-20% of energy] [26]. The Institute of Medicine of the National Academy of Sciences in the U.S. has determined that the Acceptable Macronutrient Distribution Ranges (AMDRs) for total protein at 10-35 percent of total calories for adults (aged ≥ 19 years) and at 10-30 percent of total calories for children (aged 4-18 years) and 5-20 percent of total calories for children (aged 1-3 years) [27]. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended the Protein/Energy is 10-15% of total energy (calories).

The population-based cohort study in a Chinese adult population (aged 45-74 years) revealed that the daily total protein intake of subjects with gout was significantly higher than that of subjects without gout (subjects with gout: 15.4±2.5% energy; subjects without gout: 15.2±2.4% energy) and the daily soy protein intake of subjects with gout tended to decrease compared to that of subjects without gout (subjects with gout: 1.47±0.99% energy; subjects without gout: 1.50±1.01% energy) [74]. The daily total protein intake (the mean ratio of energy intake from protein in total energy intake) of Japanese adult population (aged ≥ 20 years) was 15.2% of energy. The daily total protein intake of Japanese adult population (aged ≥ 20 years) was as same as that of Chinese adult population without gout (aged 45-74 years).

The ingestion of milk proteins (casein, lactalbumin) has been shown to exert a uricosuric effect in healthy subjects [78, 81]. The Protein/Energy seems to be appropriate or it seems better to increase it slightly. Increase in intake of animal protein from low-fat dairy products (e.g., casein, lactalbumin) and vegetable sources of protein (e.g., wheat gluten, rice endosperm protein) in Japanese people seems to be important for the prevention of gout.

3.3.4. Fats

Total Fat

The daily total fat intake of Japanese people in 2022 was higher compared to that in 1960, 1965, 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1960: 24.7 g/day; 1965: 36.0 g/day; 1975: 52.0 g/day; 1986: 56.6 g/day; 1989: 58.9 g/day; 1992: 58.4 g/day; 1995: 59.9 g/day; 1998: 57.9 g/day; 2001: 55.3 g/day; 2004: 54.1 g/day; 2007: 55.1 g/day; 2010: 53.7 g/day; 2013: 55.0 g/day; 2016: 57.2 g/day; 2019 61.3 g/day; 2022: 61.7 g/day). The daily intake of total fat did not show a significant correlation with the number of gout patients in 1986-2019 (r= -0.210, p= 0.512) and in 1986-2022 (r= 0.0549, p= 0.859).

The daily total fat intake of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 61.2 g/day; 2022: 61.5 g/day). The daily intake of total fat was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.904, p= 0.0133) and in 2004-2022 (r= 0.941, p= 0.00159).

The daily total fat intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 66.3 g/day; 2022: 66.7 g/day, women: 2019: 56.7 g/day; 2022: 57.0 g/day). The daily intake of total fat was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.912, p= 0.0113) and in 2004-2022 (r= 0.944, p= 0.0014). The daily intake of total fat did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.437, p= 0.387) and in 2004-2022 (r= -0.250, p= 0.588). This result suggests that the correlation of daily total fat intake with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The daily total fat intake of Japanese men (aged ≥ 15 years) in 2022 was higher compared to that in 2016 and was about the same as that in 2019 (2016: 52.7-76.6 g/day; 2019: 56.4-84.4 g/day; 2022: 61.1-84.3 g/day). The daily total fat intake of Japanese women (aged ≥ 20 years) in 2022 was higher compared to that in 2016 and was about the same as that in 2019 (2016: 46.4-55.9 g/day; 2019: 51.3-59.1 g/day; 2022: 52.4-58.9 g/day). The Ministry of Health, Labour and Welfare in Japan [26] has not set the Recommended Dietary Allowances (RDAs) for the daily total fat intake in Japanese people. The Estimated Average Requirement (EAR), Recommended Dietary Allowances (RDAs), the Adequate Intakes (AIs), and the Tolerable Upper Intake Levels (ULs) for total fat for individuals aged 1 year and older in the U.S. established by the Institutes of Medicine has not been set [27, 68].

In epidemiological studies, increased intake of fat was associated with increased SUA concentrations [51].

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that no statistical difference was found about the associations of dietary total fat intake with SUA concentrations [31]. A cross-sectional study from China showed that every 10 g increase in energy-adjusted fat intakes caused a 10% increase in hyperuricemia risk [32].

Animal Fat

The daily animal fat intake of Japanese people in 2022 was higher compared to that in 1972, 1975, 1980, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, and 2016 and was lower compared to that in 2019 (1972: 27.0 g/day; 1975: 27.4 g/day; 1980: 26.9 g/day; 1986: 27.9 g/day; 1989: 28.3 g/day; 1992: 28.5 g/day; 1995: 29.8 g/day; 1998: 29.2 g/day; 2001: 27.2 g/day; 2004: 26.8 g/day; 2007: 27.7 g/day; 2010: 27.1 g/day; 2013: 28.1 g/day; 2016: 29.1 g/day; 2019: 32.4 g/day; 2022: 32.3 g/day). The daily animal fat intake did not show a significant correlation with the number of gout patients in 1986-2019 (r= 0.242, p= 0.339) and in 1986-2022 (r= 0.433, p= 0.139).

The daily animal fat intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 31.9 g/day; 2022: 31.7 g/day). The daily animal fat intake was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.921, p= 0.00905) and in 2004-2022 (r= 0.949, p= 0.00109).

The daily animal fat intake of Japanese adult men (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 35.2 g/day; 2022: 34.8 g/day). The daily animal fat intake of Japanese adult women (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 28.9 g/day; 2022: 29.0 g/day). The daily animal fat intake was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.921, p= 0.00919) and in 2004-2022 (r= 0.947, p= 0.0012). The daily animal fat intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.446, p= 0.375) and in 2004-2022 (r= -0.259, p= 0.575). This result suggests that the correlation of daily animal fat intake with the number of gout patients varies with gender and is stronger in adult men than in adult women.

Vegetable Fat

The vegetable fat is from grains, potatoes, legumes, seeds, nuts, fruit, vegetables, mushrooms, and seaweed.

The daily vegetable fat intake of Japanese people in 2022 was lower compared to that in 1989, 1992, and 1995 and was higher compared to that in 1986, 1998, 2007, 2010, 2013, 2016, and 2019 (1986: 28.7 g/day; 1989: 30.6 g/day; 1992: 29.9 g/day; 1995: 30.2 g/day; 1998: 28.7 g/day; 2007: 27.3 g/day; 2010: 26.7 g/day; 2013: 26.9 g/day; 2016: 28.1 g/day; 2019: 28.9 g/day; 2022: 29.4 g/day). The daily intake of vegetable fat was negatively correlated with the number of gout patients in 1986-2019 (r= -0.676, p= 0.0157). Whereas the daily intake of vegetable fat did not show a significant correlation with the number of gout patients in 1986-2022 (r= -0.502, p= 0.0807).

The daily vegetable fat intake of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 29.3 g/day; 2022: 29.8 g/day). The daily intake of vegetable fat was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.835, p= 0.0388) and in 2004-2022 (r= 0.900, p= 0.00568).

The daily vegetable fat intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 31.1 g/day; 2022: 31.9 g/day, women: 2019: 27.7 g/day; 2022: 28.0 g/day). The daily intake of vegetable fat was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.872, p= 0.0235) and in 2004-2022 (r= 0.917, p= 0.00364). The daily intake of vegetable fat did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.371, p= 0.470), and in 2004-2022 (r= -0.199, p= 0.669). This result suggests that the correlation of daily vegetable fat intake with the number of gout patients varies with gender and is stronger in adult men than in adult women.

Saturated Fatty Acids

The daily intake of saturated fatty acids (SFAs) of Japanese in 2022 was lower compared to that in 1995 and was higher compared to that in 1998, 2002, 2005, 2007, 2010, 2013, and 2016 and was about the same as that in 2019 (1995: 18.4 g/day; 1998: 17.7 g/day; 2002: 14.3 g/day; 2005: 14.8 g/day; 2007: 15.0 g/day; 2010: 14.7 g/day; 2013: 15.1 g/day; 2016: 15.7 g/day; 2019: 18.3 g/day; 2022: 18.34 g/day). The daily intake of SFAs did not show a significant correlation with the number of gout patients in 2007–2019 (r= 0.855, p= 0.0650). Whereas the daily intake of SFAs was positively correlated with the number of gout patients in 2007-2022 (r= 0.911, p= 0.0116).

The daily intake of SFAs of Japanese adult population (aged ≥ 20 years) in 2022 was about the same as that in 2019 (2019: 17.9 g/day; 2022: 17.92 g/day). The daily intake of SFAs was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2007–2019 (r= 0.890, p= 0.0431) and in 2007-2022 (r= 0.932, p= 0.00679).

The daily intake of SFAs of Japanese adult men (aged ≥ 20 years) in 2022 was about the same as that in 2019 (2019: 19.1 g/day; 2022: 19.12 g/day) The daily intake of SFAs of Japanese adult women (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 16.7 g/day; 2022: 16.90 g/day). The daily intake of SFAs was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2007–2019 (r= 0.883, p= 0.0459) and in 2007-2022 (r= 0.927, p= 0.00789). The daily intake of SFAs did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2007-2019 (r= -0.300, p= 0.624) and in 2007-2022 (r= 0.015, p= 0.977). This result suggests that the correlation of daily intake of SFAs with the number of gout patients is stronger in adult men than in adult women.

The Estimated Average Requirement (EAR), the Recommended Dietary Allowances (RDAs), the Adequate Intakes (AIs), and the Tolerable Upper Intake Levels (ULs) for SFAs in the U.S. population established by the Institutes of Medicine has not been set [27, 68]. The Institute of Medicine of The National Academy in the U.S. has stated that recommendation for SFAs is as low possible while consuming a nutritionally adequate diet [27]. The Institute of Medicine of The National Academy in the U.S. has not been set the EAR and the RDAs for SFAs [27].

Foods high in SFAs are as follows: oil (coconut oil, palm kernel oil, palm oil), coconut powder, butter (unfermented butter, fermented butter), shortening, beef tallow, lard, meat (beef: rib roast, rib loin, shoulder, thigh, pork: loin, shoulder, thigh), margarine, cream, natural cheese, white chocolate [28, 29].

Japanese adult men (aged 20-49 years) and women (aged ≥ 20 years) should reduce the daily intake of SFAs for the prevention of gout.

Ratio of Energy Intake from Saturated Fatty Acids in Total Energy Intake

The mean ratio of energy intake from saturated fatty acids in total energy intake (SFAs/Energy) of Japanese people in 2022 was higher compared to that in 2016 and 2019 (2016: 7.54% of energy, 2019: 8.60% of energy; 2022: 8.74% of energy). The SFAs/Energy did not show a significant correlation with the number of gout patients in 2007-2016 (r=0.889, p= 0.111). Whereas the SFAs/Energy was positively correlated with the number of gout patients in 2007-2019 (r= 0.907, p= 0.0334) and in 2007-2022 (r= 0.943, p= 0.00474).

The SFAs/Energy of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 8.39% of energy; 2022: 8.51% of energy). The SFAs/Energy was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2007-2019 (r= 0.921, p= 0.0266) and in 2007-2022 (r= 0.943, p= 0.00474).

The SFAs/Energy of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 8.05% of energy; 2022: 8.15% of energy, women: 2019: 8.77% of energy; 2022: 8.88% of energy). The SFAs/Energy was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2007-2019 (r= 0.906, p= 0.0340) and in 2007-2022 (r= 0.940, p= 0.00525). The SFAs/Energy did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2007-2019 (r= -0.368, p= 0.642) and in 2007-2022 (r= -0.029, p= 0.956). This result suggests that the correlation of SFAs/Energy with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The SFAs/Energy of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 8.08-9.27% of energy and 8.43-9.74% of energy, respectively, and exceeded the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan (men and women: 15-17 years: ≤ 8% of energy; ≥ 18 years: ≤ 7% of energy) [26]. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended SFAs/Energy is < 10% of total energy (calories).

This result suggests that decrease in intake of SFAs in Japanese people (aged ≥ 15 years) is important for prevention of gout.

Monounsaturated Fatty Acids

The daily intake of monounsaturated fatty acids (MUFAs) of Japanese people in 2022 was higher than that in 2007, 2010, 2013, 2016, and 2019 (2007: 18.70 g/day; 2010: 18.33 g/day; 2013: 18.82 g/day; 2016: 19.70 g/day; 2019: 22.50 g/day; 2022: 22.71 g/day). The daily intake of MUFAs did not show a significant correlation with the number of gout patients in 2007-2019 (r= 0.860, p= 0.0617). Whereas the daily intake of MUFAs was positively correlated with the number of gout patients in 2007-2022 (r= 0.915, p= 0.0106).

The daily intake of MUFAs of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 22.53 g/day; 2022: 22.67 g/day). The daily intake of MUFAs was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2007-2019 (r= 0.883, p= 0.0460) and in 2007-2022 (r= 0.929, p= 0.00733).

The daily intake of MUFAs of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019 (men: 2019: 24.70 g/day; 2022: 24.83 g/day, women: 2019: 20.63 g/day; 2022: 20.81 g/day). The daily intake of MUFAs was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2007-2019 (r= 0.880, p= 0.0488) and in 2007-2022 (r= 0.924, p= 0.00843). The daily intake of MUFAs did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2007-2019 (r= -0.314, p=0.0607) and in 2007-2022 (r= 0.00432, p= 0.994). This result suggests that the correlation of daily intake of MUFAs with the number of gout patients varies with gender and is stronger in adult men than in adult women.

Polyunsaturated Fatty Acids

The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of polyunsaturated fatty acids (PUFAs) is 6-10% of total energy (calories). The Ministry of Health, Labour and Welfare of Japan [26] has not set the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) for the daily intake of n-3 polyunsaturated fatty acids (n-3 PUFAs) and n-6 polyunsaturated fatty acids (n-6 PUFAs) in Japanese men and women. The Estimated Average Requirement (EAR), the Recommended dietary allowances (RDAs), and the Tolerable Upper Intake Levels (ULs) for n-3 PUFAs and n-6 PUFAs in the U.S. population established by the Institutes of Medicine has not been set [27, 68].

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2003-2015) data collected for 26323 subjects (13003 men and 13320 women) (aged ≥ 20 years) showed that higher intake of n-3 PUFAs, α-linolenic acid (ALA), n-6 PUFAs, linoleic acid, and non-marine PUFAs were associated with decreased hyperuricemia risk [hyperuricemia: SUA concentration > 420.0 μmol/L in men and > 360.0 μmol/L in women] [82]. Detailed results are shown in the following sections. Replacing 5% of total energy intake from saturated fatty acids with isocaloric PUFAs was associated with decreased hyperuricemia risk [82]. Aa a possible mechanism, Chen et al. [82] have stated that insulin resistance, which leads to hyperuricemia by reducing UA excretion and activating xanthine oxidoreductase, is alleviated by replacing 5%-7.5% of total energy from SFAs with isocaloric PUFAs or n-6 PUFAs, or by administering a diet enriched in n-3 PUFAs.

Zhang et al. [83] found that higher n-3:n-6 ratio foods such as fatty fish was associated with lower risk of gout flares, more neutral n-3:n-6 ratio foods such as spinach had no effect on out flare risk, and lower n-3:n-6 ratio foods such as egg was associated with increased risk of gout flares.

Many epidemiological studies and clinical trials are needed to examine the effect of polyunsaturated fatty acids in the management of gout.

n-3 polyunsaturated fatty acids

The daily intake of n-3 polyunsaturated fatty acids (n-3 PUFAs) of Japanese people in 2022 was lower than that in 2007 and 2019 and was higher than that in 2013 and 2016 and was the same as that in 2010 (2007: 2.37 g/day; 2010: 2.24 g/day; 2013: 2.17 g/day; 2016: 2.16 g/day; 2019: 2.36 g/day; 2022: 2.24 g/day). The daily intake of n-3 PUFAs did not show a significant correlation with the number of gout patients in 2007-2019 (r= -0.0978, p= 0.876) and in 2007-2022 (r= -0.132, p= 0.803).

The daily intake of n-3 PUFAs of Japanese adult population (aged ≥ 20 years) in 2022 was lower than that in 2019 (2019: 2.46 g/day; 2022: 2.33 g/day). The daily intake of n-3 PUFAs did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2007-2019 (r= -0.0876, p= 0.889) and in 2007-2022 (r= -0.132, p= 0.803).

The daily intake of n-3 PUFAs of Japanese adult men (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 2.68 g/day; 2022: 2.57 g/day). The daily intake of n-3 PUFAs of Japanese adult women (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 2.27 g/day; 2022: 2.12 g/day). The daily intake of n-3 PUFAs did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2007-2019 (r= -0.220, p= 0.723) and in 2007-2022 (r= -0.220, p= 0.675). The daily intake of n-3 PUFAs did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2007-2019 (r= 0.130, p= 0.835) and in 2007-2022 (r= 0.065, p= 0.902).

The daily intake of n-3 PUFAs for men (aged ≥ 15 year) and women (aged ≥ 15 years) in 2022 were 2.29-2.91 g/day and 1.74-2.43 g/day, respectively, and exceeded the Adequate Intakes (AIs) established by the Ministry of Health, Labour and Welfare in Japan [men (aged ≥ 15 years): 2.0-2.2 g/day; women (aged ≥ 7 years): 1.6-2.0 g/day] [26]. This result suggests that the daily intake of n-3 PUFAs in Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) appears to be very unlikely to cause a deficiency. The Estimated Average Requirement (EAR) and the Recommended Dietary Allowances (RDAs) for n-3 PUFAs in the U.S. population established by the Institutes of Medicine has not been established [27, 68]. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of n-3 PUFAs is 1-2% of total energy (calories). The Institute of Medicine of the National Academy of Sciences in the U.S. has determined that the Acceptable Macronutrient Distribution Ranges (AMDRs) for n-3 polyunsaturated fatty acids (α-linolenic acid) both adults (aged ≥ 19 years) and children (aged 4-18 years) is 0.6-1.2 percent of total calories [27]. The Institute of Medicine of the National Academy of Sciences in the U.S. has established that the AIs for α-linolenic acid is 1.2-1.6 g/day for males (aged ≥ 9 years) and 1.0-1.1 g/day for females (aged ≥ 9 years), respectively [males (aged 9-13 years): 1.2 g/day; males (aged ≥ 14 years): 1.6 g/day; females (aged 9-13 years): 1.0 g/day; females (aged ≥ 14 years): 1.1 g/day] [27].

The n-3 PUFAs are known for their powerful anti-inflammatory effects [84]. Anti-inflammatory effects of n-3 PUFAs in experimental gout in mice or rats are presented below. Omega-3-carboxylic acids [purified eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), palmitic acid, and oleic acid] reduced interleukin-1β (IL-1β) and prostaglandin E2 production, exudate volume, and white blood cell (WBC) infiltration in rat monosodium urate (MSU) crystal air pouch model and inhibited pain and swelling in rat knee intra-articular MSU injection model, suggesting omega-3-carboxylic acids has anti-inflammatory effects [85]. Yan et al. [86] found that DHA prevents inflammation and metabolic disorder through inhibition of nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome activation in mice. Diets enriched in both linolenic acid and EPA significantly suppressed urate crystal-induced inflammation in a rat model [87]. EPA and DHA inhibit pathways like toll-like receptor activation, NALP-3 inflammasome assembly, neutrophil chemotaxis, prostaglandin synthesis and nucleating factor-kB activity through which MSU crystals induce inflammation [84]. These n-3 PUFAs show a potential protective role against gout flares.

A cross-sectional study using US NHANES (2003-2015) showed that US adults in the highest quartile of intake of n-3 PUFAs and α-linolenic acid (ALA) were 23.0% and 31.0% less likely to be hyperuricemia [hyperuricemia: SUA concentration ≥ 420 μmol/L in men and ≥ 360 μmol/L) in women] compared to those subjects in the lowest quartile of intake of each PUFAs, respectively [82]. As one of possible mechanisms of the association between n-3 PUFAs intake and hyperuricemia, The *in vitro* study showed that EPA, ALA, and DHA strongly inhibited urate transporter 1 (URAT1), which are UA reabsorption proteins, activities and n-3 PUFAs inhibited the function of URAT 1 more effectively than saturated fatty acids (SFAs) [88]. Saito et al. [88] have stated that n-3 PUFAs can be employed as uricosuric agents. The n-3 PUFAs will be preferable nutrients for the prevention of hyperuricemia/gout.

The results of a recently clinical trial are presented below. A randomized controlled trial in 74 healthy men and women for 6 weeks showed that intervention with ALA, EPA, or DHA diets did not significantly decrease plasma UA concentrations [89]. Whereas mean plasma UA concentrations of ALA, EPA, or DHA group at baseline (ALA: 239 μmol/L; EPA: 264 μmol/L; EPA: 240 μmol/L) and 6- week intervention (ALA: 231 μmol/L; EPA: 247 μmol/L; EPA: 232 μmol/L) were within the normal physiological range [2.0-7.0 mg/dL (119.0-416.4 μmol/L) for men and 2.0-6.5 mg/dL (119.0-386.7 μmol/L) for women [90]], respectively. A randomized controlled trial involving 30 Chinese participants for 8 weeks showed that intake of fish oil increased plasma saturated fatty acids and n-3 PUFAs concentrations and decreased plasma n-6 PUFAs, UA, triacylglycerol, C-reactive protein, and ferritin concentrations compared with baseline [91]. In a case-control study, Li et al. [92] observed a negative association between plasma DHA and plasma UA concentrations. On the contrary, A randomized controlled trial involving 34 male overweight subjects showed that a ketogenic Mediterranean diet with n-3 PUFAs for 4 weeks had no effect on UA concentration [93]. From results of these reports, Chen et al. [82] have stated that the inconsistency on the effect of n-3 PUFAs on serum or plasma UA concentrations may stem from variations in the composition or dosage of n-3 PUFAs.

In a pilot randomized open-label clinical trial in patients with gout (aged ≥ 18 years) for 6 months, no significant differences were detected in the SUA concentrations and the percentage of participants experiencing at least one flare each month between omega-three fish oil (6.2 g of omega-3 fatty acids per day) supplementation and controls for intervention periods, respectively [94]. However, red cell omega-3 concentrations significantly correlated with the number of gout flare-ups [94]. Abhishek et al. [84] found that low serum levels of n-3 PUFAs were associated with frequent gout attacks. In a cohort study on 724 gout patients, intake of n-3 PUFA rich fatty fish was associated with a lower risk of gout flare-up, while intake of n-3 PUFA rich supplements did not reduce the risk of gout flares recurrence [83].

Nuts and seeds contain rich in n-3 polyunsaturated fatty acids (ALA) [28, 30]. Fatty fish, such as tuna, mackerel, and salmon, contains rich in n-3 polyunsaturated fatty acids [EPA and DHA] [28, 30]. Foods high in ALA, EPA and DHA are as follows: oil (flaxseed oil, canola oil, soybean oil), seeds and nuts (chia seeds, English walnuts, flaxseed, black walnuts), seafood (salmon, herring, sardines, mackerel, trout, oysters, sea bass, shrimp, lobster, tuna, tilapia, scallops, cod), legumes (edamame, refried beans, kidney beans, baked beans), meat (ground beef, chicken breast), bread, egg, low-fat milk, mayonnaise [95]. One should consume at least 250 mg/day of long-chain n-3 PUFAs or at least 2 servings/week of oily fish [96].

It seems important for Japanese people to eat fatty fish, nuts, and seeds to take in more n-3 PUFAs for the prevention and management of gout.

n-6 polyunsaturated fatty acids

The daily intake of n-6 polyunsaturated fatty acids (n-6 PUFAs) of Japanese people in 2022 was higher compared to that in 2007, 2010, 2013, 2016, and 2019 (2007: 9.45 g/day; 2010: 9.27 g/day; 2013: 9.28 g/day; 2016: 9.61 g/day; 2019: 10.50 g/day; 2022: 10.78 g/day). The daily intake of n-6 PUFAs did not show a significant correlation with the number of gout patients in 2007–2019 (r= 0.776, p= 0.123). Whereas the daily intake of n-6 PUFAs was positively correlated with the number of gout patients in 2007-2022 (r= 0.867, p= 0.0252).

The daily intake of n-6 PUFAs of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2016 and 2019 (2016: 9.73 g/day; 2019: 10.66 g/day; 2022: 10.88 g/day). The daily intake of n-6 PUFAs did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2007–2019 (r= 0.820, p= 0.0890). Whereas the daily intake of n-6 PUFAs was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2007-2022 (r= 0.893, p= 0.0166).

The daily intake of n-6 PUFAs of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 11.61 g/day; 2022: 11.90 g/day, women: 2019: 9.84 g/day; 2022: 10.00 g/day). The daily intake of n-6 PUFAs did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2007–2019 (r= 0.837, p= 0.0769). Whereas the daily intake of n-6 PUFAs was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2007-2022 (r= 0.896, p= 0.0156). The daily intake of n-6 PUFAs did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2007-2019 (r= -0.323, p= 0.596) and in 2007-2022 (r= 0.022, p= 0.968). This result suggests that the correlation of daily intake of n-6 PUFAs with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The daily intake of n-6 PUFAs of Japanese men (aged 15-19 years), men (aged ≥ 20 years), women (aged 15-19 years), and women (aged ≥ 20 years) in 2022 were 14.59 g/day, 10.41-12.76 g/day, 10.85 g/day, and 9.03-10.63 g/day, respectively, and exceeded the Adequate Intakes (AIs) established by the Ministry of Health, Labour and Welfare in Japan [men (aged 15-17 years): 13.0 g/day; men (aged 18-29 years): 11.0 g/day; men (aged ≥ 30 years): 8.0-10.0 g/day; women (aged 15-17 years): 9.0 g/day; women (aged 18-74 years): 8.0 g/day; women (aged ≥ 75 years): 7.0 g/day] [26]. The Institute of Medicine of the National Academy of Sciences in the U.S. has established that the AIs for linoleic acid is 14.0-17.0 g/day for males (aged ≥ 14 years) and 11.0-12.0 g/day for females (aged ≥ 14 years), respectively [males (aged 14-18 years): 16.0 g/day; males (aged 19-50 years): 17.0 g/day; males (aged ≥ 51 years): 14.0 g/day; females (aged 14-18 years): 11.0 g/day; females (aged 19-50 years): 12.0 g/day; females (aged ≥ 51 years): 11.0 g/day] [27]. Though n-6 PUFAs researched by the Ministry of Health, Labour and Welfare in Japan were not only linoleic acid (98%), the daily intake of n-6 PUFAs of Japanese men (aged ≥ 15 years) and Japanese women (aged ≥ 15 years) in 2022 were below the AIs established by The Institute of Medicine of the National Academy of Sciences in the U.S. Considering the AIs established by the Ministry of Health, Labour and Welfare in Japan, the daily intake of n-6 PUFAs in Japanese men and women (aged ≥ 15 years) appears to be very unlikely to cause a deficiency. However, it seems better to increase the daily intake of n-6 PUFAs slightly.

The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of n-6 PUFAs is 5-8% of total energy (calories). The Institute of Medicine of the National Academy of Sciences in the U.S. has determined that the Acceptable Macronutrient Distribution Ranges (AMDRs) for n-6 PUFAs (linoleic acid) both adults (aged ≥ 19 years) and children (aged 4-18 years) is 5-10 percent of total calories [27].

A cross-sectional study using US NHANES (2003-2015) showed that US adults in the highest quartile of intake of n-6 PUFAs and linoleic acid were 25.0% and 25.0% less likely to be hyperuricemia [hyperuricemia: SUA concentration ≥ 420 μmol/L in men and ≥ 360 μmol/L) in women] compared to those subjects in the lowest quartile of intake of each PUFAs, respectively [82]. As one of possible mechanisms of the association between PUFAs intake and hyperuricemia, Chen et al. [82] have stated that lower γ-linoleic acid (biomarker reflecting habitual consumption of n-6 PUFAs) was associated with increased abundance of gut microbiota.

Foods high in n-6 PUFAs are as follows: oil (safflower oil, grape oil, sunflower oil, cottonseed oil, corn oil, soybean oil, chili oil, sesame oil, rice bran oil, rapeseed oil), seeds and nuts (walnuts, poppy seeds, pine nuts, Brazil nuts, sunflower seeds, sesame seeds, pecans, peanuts, pistachio nuts, almonds), seafood (sardines canned, bonito canned, tuna canned), soybeans, yuba, mayonnaise [95]. It seems important for Japanese people to eat above-mentioned foods to take in more n-6 PUFAs to reach the AIs established by The Institute of Medicine of the National Academy of Sciences in the U.S.

Cholesterol

The daily intake of cholesterol of Japanese people in 2022 was lower compared to that in 1995 and 1998, and was higher compared to that in 2001, 2004, 2007, 2010, 2013, and 2016, and 2019 (1995: 383 mg/day; 1998: 370 mg/day; 2001: 346 mg/day; 2004: 320 mg/day; 2007: 323 mg/day; 2010: 307 mg/day; 2013: 307 mg/day; 2016: 311 mg/day; 2019 335 mg/day; 2022 347 mg/day). The daily cholesterol intake did not show a significant correlation with the number of gout patients in 2004-2019 (r= 0.294, p= 0.572) and in 2004-2022 (r= 0.614, p= 0.143).

The daily intake of cholesterol of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 340 mg/day; 2022 352 mg/day). The daily cholesterol intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.461, p= 0.357) and in 2004-2022 (r= 0.703, p= 0.078).

The daily cholesterol intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 366 mg/day; 2022 379 mg/day, women: 2019: 317 mg/day; 2022 328 mg/day). The daily cholesterol intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.398, p= 0.447) and in 2004-2022 (r= 0.651, p= 0.113). The daily cholesterol intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.0160, p= 0.976) and in 2004-2022 (r= 0.100, p= 0.831).

The Ministry of Health, Labour and Welfare of Japan [26] has not set an index for the daily intake of cholesterol in Japanese adults. The Estimated Average Requirement (EAR), the Recommended Dietary Allowances (RDAs), the Adequate Intakes (AIs), and the Tolerable Upper Intake Levels (ULs) for cholesterol in the U.S. population established by the Institutes of Medicine has not been set [27, 68]. The Institute of Medicine of the National Academy of Sciences in the U.S. has stated that recommendation for dietary cholesterol is as low possible while consuming a nutritionally adequate diet [27]. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended intake of cholesterol is < 300 mg/day. The mean daily intake of cholesterol of Japanese people, Japanese men (aged ≥ 20 years), and Japanese women (aged ≥ 20 years) in 2022 were 347 mg/day, 379 mg/day, and 328 mg/day, respectively, and exceeded the recommended intake of cholesterol established by The Joint WHO/FAO Expert Consultation. The Ministry of Health, Labour and Welfare in Japan [26] has stated that, for the daily cholesterol intake, it is desirable to take less than 200 mg from the viewpoint of preventing aggravation of dyslipidemia. Thus, it is important for Japanese people to reduce daily cholesterol intake to prevent the aggravation of dyslipidemia. It seems that decreasing intake of cholesterol and/or avoidance of excessive intake of cholesterol in Japanese adults is important for the prevention of lifestyle-related diseases including gout.

The results of a recently published article are presented below. A cross-sectional study using US NHANES (2017-2018) data showed that no statistical difference was found about the associations of dietary cholesterol intake with SUA concentrations [31].

Foods high in cholesterol are as follows: liver, egg yolk, dried herring roe, dried squid, anchovy, sardines, shrimp, abalone, salmon, mackerel, sea urchin, carp, sweet fish, lobster, full-fat dairy products [27, 28].

Ratio of Energy Intake from Fat in Total Energy Intake

The mean ratio of energy intake from fat in total energy intake (Fat/Energy) of Japanese people in 2022 was higher compared to that in 1975, 1980, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1975: 22.3%; 1980: 23.6%; 1986: 24.5%; 1989: 25.7%; 1992: 25.5%; 1995: 26.2%; 1998: 26.1%; 2001: 25.2%; 2004: 25.3%; 2007: 25.8%; 2010: 25.9%; 2013: 26.2%; 2016: 27.4%; 2019: 28.6%; 2022: 29.1%). The Fat/Energy was positively correlated with the number of gout patients in 1986-2019 (r= 0.660, p= 0.0195) and in 1986-2022 (r= 0.737, p= 0.00409).

The Fat/Energy of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 28.4% of energy; 2022: 28.9% of energy). The Fat/Energy was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.953, p= 0.00328) and in 2004-2022 (r= 0.971, p= 0.00027).

The Fat/Energy of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were higher compared to those in 2019, respectively (men: 2019: 27.4% of energy; 2022: 28.1% of energy, women: 2019: 29.2% of energy; 2022: 29.5% of energy). The Fat/Energy was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.966, p= 0.00170) and in 2004-2022 (r= 0.975, p= 0.00019). The Fat/Energy did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.619, p= 0.190) and in 2004-2022 (r= -0.396, p= 0.379). This result suggests that the correlation of the Fat/Energy with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The Fat/Energy of Japanese men (aged ≥ 20 years) and women (aged ≥ 60 years) in 2022 were 25.5-29.8% of energy, and 26.4-29.6% of energy, respectively, and were within the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan [men (aged ≥ 15 year): 20-30% of energy; women (aged ≥ 15 year): 20-30% of energy] [26]. The Fat/Energy for Japanese men (15-19 years) and women (15-59 years) were 30.2% of energy and 30.3-32.4% of energy, respectively, and exceeded the DG established by the Ministry of Health, Labour and Welfare in Japan [men (aged ≥ 15 year): 20-30% of energy; women (aged ≥ 15 year): 20-30% of energy] [26]. The Institute of Medicine of the National Academy of Sciences in the U.S. has determined that the Acceptable Macronutrient Distribution Ranges (AMDRs) for total fat at 20-35 percent of total calories for adults (aged ≥ 19 years) and at 25-35 percent of total calories for children (aged 4-18 years) and 30-40 percent of total calories for children (aged 1-3 years) [27]. The mean ratio of energy intake from fat in total energy intake (Fat/Energy) of Japanese adult men (aged ≥ 20 years) and Japanese adult women (aged ≥ 20 years) in 2022 were 28.1% of energy and 29.5% of energy, respectively, and were within the AMDRs. The Joint WHO/FAO Expert Consultation [46] has stated that the recommended the Fat/Energy is 15-30% of total energy (calories). The Fat/Energy for Japanese women (15-59 years) exceeded the recommended the Fat/Energy established by the Joint WHO/FAO Expert Consultation [46]. The Fat/Energy was positively correlated with the number of gout patients in 1986-2022 (r= 0.737, p= 0.00409). It seems better to decrease the Fat/Energy.

3.3.5. Caloric Ratio of Protein, Fat, and Carbohydrate

The number of gout patients of Japanese people increased 0.052 million people from 2019 to 2022 (2019: 1.254 million; 2022: 1.306 million). Compared to the Japanese diet in 2019, in the Japanese diet in 2022, the Protein/Energy was the same and the Fat/Energy increased by 0.5% and the Carbohydrate /Energy decreased by 0.5%. The Fat/Energy in 1986-2022 and Saturated fatty acids/Energy in 2007-2022 were positively correlated with the number of gout patients, respectively. It is speculated that one of the factors contributing to the increase in the number of gout patients is the increased intake of fat, particularly saturated fatty acids.

The balance of the caloric ratio of protein, fat, and carbohydrate of Japanese people in 2022 was protein: 15.1%, fat: 29.1%, and carbohydrates: 55.8%. As described above-mentioned sections, The balance of the caloric ratio of protein, fat, and carbohydrate of Japanese people in 2022 was within the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG) established by the Ministry of Health, Labour and Welfare in Japan [26] or the Acceptable Macronutrient Distribution Ranges (AMDRs) set by the Institute of Medicine of the National Academy of Sciences in the U.S. [27]. The Ministry of Agriculture, Forestry and Fisheries in Japan [97] has stated that the ideal balance of the caloric ratio of protein, fat and carbohydrate for healthy life is protein: 15%, fat: 25%, and carbohydrate: 60%. Since the Fat/Energy of Japanese people in 2022 was 29.1%, it seems better to decrease the Fat/Energy until 20-25%.

4. Limitations

The limitations of this study are the same as those of previous studies [16, 17]. Many randomized controlled trials are required to evaluate the effect of dietary macronutrient intake on SUA concentration in patients with or without hyperuricemia and/or gout in the future. The author also hopes that the association between macronutrient intake and risk of gout will be further elucidated in large-scale prospective cohort studies.

5. Conclusions

The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2021 Gout Collaborators [1] estimates that the total number of individuals with gout worldwide increased 1.506-fold from 1990 to 2020 (55.8 million in 2020) and the age-standardized prevalence of gout in 2020 increased by 22.5% from 1990, with increases in most GBD regions. The number of gout patients of Japanese people in 2022 was higher compared to that in 2016 and 2019 (2016: 1.105 million; 2019: 1.254 million; 2022: 1.306 million) (Table 1). Almost all gout patients were adults, and the number of gout patients were higher in men than in women (Table 2). The daily intake of dietary fiber of Japanese men (aged ≥ 15 years) in 2022 was below the Adequate Intakes (AIs) established by the Institute of Medicine of the National Academy of Sciences in the U.S. The Fat/Energy and Saturated fatty acids/Energy and the daily intake of saturated fatty acids, monounsaturated fatty acids, and n-6 polyunsaturated fatty acids were positively correlated with the number of gout patients in Japanese people, respectively (Table 3). Whereas the daily intake of total carbohydrate was negatively correlated with the number of gout patients in Japanese people (Tables 3). Similar tendencies were observed in Japanese adult population (aged ≥ 20 years) and adult men (aged ≥ 20 years) (Table 4).

As the previous report [16, 18], this article also suggests the importance of macronutrient for the prevention of gout in Japanese people referencing the results of clinical research reported. Modification of macronutrient intake for the prevention of gout in Japanese people (especially adults) in 2022 is suggested as follows: 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, saturated fatty acids, cholesterol; increase intake of carbohydrate (particularly dietary fiber) and protein (particularly animal protein from low-fat dairy products and vegetable protein). Contents of modification of macronutrient intake for the prevention of gout in Japanese people (especially adults) in 2022 were almost the same as those in 2019. Considering daily protein intake and protein source and choosing foods containing protein is important for Japanese people for the prevention of gout; that is to say, decreasing the intake of protein foods rich in fat, especially saturated fatty acids and cholesterol, and increasing the intake of vegetable protein (e.g., wheat gluten, rice endosperm protein) and choosing low-fat dairy products may lead to a decrease in fat intake and an increase in carbohydrate intake. Intake of animal protein from low-fat dairy products (e.g., casein, lactalbumin), vegetable protein (e.g., wheat gluten, rice endosperm protein) and carbohydrate (particularly dietary fiber) in Japanese people seems to be important for the prevention of gout.

The important points of macronutrient intake for the prevention and management 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.; decrease the mean ratio of energy intake from saturated fatty acids in total energy intake (Saturated fatty acids/Energy) within the range of the 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 free sugars, fructose, and sucrose); limiting alcohol consumption; and maintenance of good hydration. It is necessary to recognize what micronutrient (vitamin and mineral) intake is important as potential dietary habits to prevent gout in Japanese people.

There is a lack of clinical trials that have investigated the effect of dietary factors or foods on SUA concentrations and the risks of hyperuricemia and gout, and thus randomized controlled trials are needed to establish causal relationships. Furthermore, as shown in the previous article [98], there are several reports about the effects of dietary patterns on SUA concentrations. Further research is necessary to assess to what extent SUA concentrations change by the differences in dietary patterns under isocaloric feeding conditions in individuals without and with hyperuricemia or gout.

Abbreviations

AI	Adequate Intake
AMDRs	Acceptable Macronutrient Distribution Ranges
DHA	Docosahexaenoic Acid
EPA	Eicosapentaenoic Acid
EAR	Estimated Average Requirement
Carbohydrate /Energy	Mean Ratio of Energy Intake from Carbohydrate in Total Energy Intake
Fat/Energy	Mean Ratio of Energy Intake from Fat in Total Energy Intake
Protein/Energy	Mean Ratio Of Energy Intake From Protein In Total Energy Intake
SFAs /Energy	Mean Ratio of Energy Intake from Saturated Fatty Acids in Total Energy Intake
MSU	Monosodium Urate
MUFAs	Monounsaturated Fatty Acids
NHANES	National Health and Nutrition Examination Survey
RDA	Recommended Dietary Allowance
SFAs	Saturated Fatty Acids
SUA	Serum Uric Acid
GBD	The Global Burden of Diseases, Injuries, and Risk Factors Study
UL	Tolerable Upper Intake Level
SUA	Uric Acid
n-3 PUFAs	n-3 polyunsaturated Fatty Acids
n-6 PUFAs	n-6 polyunsaturated Fatty Acids
ALA	α-linolenic Acid

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Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

Takashi Koguchi is a visiting professor at Kokugakuin University Tochigi Junior College, Department of Human Education. He completed his PhD in Agricultural Chemistry from Tokyo University of Agriculture in 2007, and his Master of Agricultural Chemistry from the same institution in 1992. He served on the Special Editorial Boards of International Journal of Food Science and the Reviewers of International Journal of Nutrition and Food Sciences. He currently serves on the Editorial Boards of American Journal of Health Research.

Research Field

Takashi Koguchi: Nutrition, Agricultural Chemistry, Health Care, Biomedicine, Agricultural Chemistry, Pharmacology, Physiology, Food Chemistry.