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Research Article

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

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Abstract

The number of gout patients of Japanese people increased 5.12-fold from 1986 to 2022 (1986: 0.255 million; 2022: 1.306 million). The aim of this article is to suggest what micronutrient intake is important for the prevention of gout in Japanese people in 2022 referencing the results of clinical research reported. The author used the data of the Comprehensive Survey of Living Conditions in Japan for the number of gout patients (1986-2022) and the data of the National Health and Nutrition Survey in Japan (1946-2022) for the intake of micronutrients. Micronutrient intake of Japanese people in 2022 were compared with those in 2019. The relationship between the number of gout patients and micronutrient intake in Japanese people was examined. The daily intake of micronutrients of Japanese people in 2022 were evaluated using Dietary Reference Intakes. The daily intake of vitamin E, vitamin K, and pantothenic acid of Japanese people in 2022 were higher compared to those in 2019, respectively. Whereas the daily intake of vitamin A, vitamin D, vitamin B_2, niacin, vitamin B_6, folate, vitamin B_{12}, vitamin C, sodium, salt, calcium, potassium, magnesium, phosphorus, iron, copper, and zinc of Japanese people in 2022 were lower compared to those in 2019. The daily intake of vitamin B_1 of Japanese people in 2022 was the same as that in 2019. The daily intake of vitamin A, vitamin D, vitamin E, vitamin B_1, vitamin B_2, folate, vitamin B_{12}, vitamin C, salt, calcium, iron, and copper were negatively correlated with the number of gout patients, respectively. The daily niacin intake was positively correlated with the number of gout patients. Modification of micronutrient intake for the prevention of gout in Japanese people (especially adults) in 2022 is suggested as follows: limiting or decreasing intake of sodium and salt; decreasing intake of niacin; decreasing or pay attention to not to excessive intake of vitamin K, pantothenic acid, vitamin B_{12}, phosphorus, and copper; increase intake of vitamin A, vitamin D, vitamin E, vitamin B_1, vitamin B_6, folate, calcium, potassium, and magnesium; increase intake of vitamin B_2 in Japanese men (aged 15-59 years) and women (aged 15-49 years), vitamin C in Japanese men (aged 20-59 years) and women (aged 20-49 years), iron in Japanese men (aged 20-59 years) and women (aged 20-69 years, ≥ 75 years), and zinc in Japanese men (aged ≥ 20 years) and women (aged 20-69 years, aged ≥ 80 years).

Keywords

Antioxidant, Dietary Reference Intakes, Gout, Hyperuricemia, Mineral, Uric Acid, Vitamin

1. Introduction

Gout is the most common form of inflammatory arthritis, and it is characterized by the deposition of monosodium urate (MSU) crystals that form in the presence of increased uric acid (UA) concentrations [1]. UA possesses antioxidant,

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pro-oxidative, pro-inflammatory, nitric oxide modulating, anti-aging, and immune effects, which are significant in both physiological and pathological contexts [2]. UA can promote metabolic inflammation and trigger the release of some key pro-inflammatory cytokines [3]. The serum uric acid (SUA) concentrations have been associated with several inflammatory markers [neutrophil count, C-reactive protein (CRP), interleukin-1 receptor antagonist (IL-1ra), interleukin-6 (IL-6), interleukin-18 (IL-18), tumor necrosis factor-alpha (TNF-α)] in individuals with or without hyperuricemia [SUA concentration > 7.5 mg/dL (450 μmol/L) in men and > 6.2 mg/dL (372 μmol/L) in women] [4]. A high SUA concentration (hyperuricemia) is frequently associated with 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 [6]. The typical damage caused by asymptomatic hyperuricemia includes inflammation, oxidative stress and gut dysbiosis [7]. Hyperuricemia can trigger inflammation during the pathogenesis of acute gout as nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome and interleukin were activated [8].

UA can exert, along with its extracellular antioxidant activity, an intracellular prooxidant effect [9]. The lower 1/3 of the normal physiological range (2.0-4.0 mg/dL: 119.0-237.9 μmol/L) and elevations of > 4 mg/dL (> 237.9 μmol/L) in SUA concentrations are antioxidant and conditional prooxidant, respectively [10]. The xanthine oxidoreductase activities are the purine catabolism, which generates UA, and the regulation of cell redox state and cell signaling, through the production of reactive oxygen species (ROS) [11]. UA releases free radicals and deactivate innate antioxidant enzymes to exacerbate oxidative stress, leading to hyperuricemia [12]. Sustained hyperuricemia can cause an imbalance of free radicals and antioxidative enzymes in the body, which is closely correlated to the occurrence of oxidative stress [13]. Hyperuricemia associated with oxidative stress is incriminated in DNA damage, oxidations, inflammatory cytokine production, and even cell apoptosis [14]. Hyperuricemia exacerbates oxidative stress, thereby intensifying inflammation and endothelial dysfunction within this context and accelerates arteriosclerosis [2]. Oxidative stress is also a characteristic feature of chronic kidney disease (CKD) [2]. Hyperuricemia is linked to a spectrum of commodities such as gout [2, 15], hypertension [2, 15], cardiovascular disease (CVD) [2, 15], renal disease [2, 15], metabolic syndrome [2], and diabetes mellitus [2]. In the US National Health and Nutrition Examination Survey (NHANES) 2007-2008, the comorbidities of individuals with hyperuricemia, gout, or both hyperuricemia and gout were hypertension, CKD, obesity (body mass index: BMI ≥ 30 kg/m^2), diabetes mellitus, nephrolithiasis, and CVD (myocardial infarction, heart failure, stroke) [1]. Free radicals or reactive species through oxidative stress have been evidently implicated in the incidence and progression of arteriosclerosis, diabetes mellitus, CVD, cancer, neurodegenerative disorders [16]. Decrease in SUA concentrations in individuals with hyperuricemia is important for the prevention or management of hyperuricemia and gout and their comorbidities (e.g., CKD, hypertension, diabetes mellitus, CVD).

Vitamin A, vitamin E, and vitamin C are nonenzymatic antioxidants [10] and show beneficial effects against oxidative stress and inflammation, as well as effectively decreasing SUA levels [17-19]. The mechanism of lowering SUA level was because of the antioxidant activity of these nutrients (e.g., vitamin C, vitamin E, polyphenols, carotenoids) which could reduce oxidative stress and further decrease UA synthesis [20, 21]. Defenses against free radical damage include several metalloenzymes including glutathione peroxidases (selenium), catalase (iron), and superoxide dismutase (copper, zinc, manganese) and ceruloplasmin (copper) [22]. The cross-sectional studies showed that increased dietary antioxidant intake was associated with decreased SUA concentrations or decreased hyperuricemia risk; that is to say, increased intake of vitamin C [20, 23-25] was associated with decreased SUA concentrations and increased intake of retinol [26], vitamin E [17], vitamin C [23, 25, 27, 28], and zinc [21] were associated with decreased hyperuricemia risk. Vitamin D and vitamin D receptor signaling together have a suppressive role on autoimmunity and an anti-inflammatory effect [29]. Vitamin D intake was inversely associated with hyperuricemia risk [30]. Serum 1,25-dihydroxy vitamin D3 levels was negatively correlated with serum C-reactive protein (CRP) levels in gout arthritis patients [31]. This suggests that vitamin D3 plays a protective role in gout. Individuals with gouty arthritis had higher intakes of energy, protein, carbohydrate, fat, fructose, vitamin C, and vitamin B_{12} and consumed more alcohol [32]. These reports suggest that recognizing the daily intake of nutrients (especially antioxidant, vitamin D) in Japanese people is necessary factor to prevent gout through lowering SUA levels.

The number of gout patients of Japanese people in 2022 was higher compared to that in 2019 and increased 5.12-fold compared to that in 1986 (1986: 0.255 million; 2019: 1.254 million; 2022: 1.306 million) [33-35]. The objective of this article is to propose a preventive method for gout through the evaluation of recent dietary habits in Japanese people. Therefore, it is necessary to recognize what and how much nutrient intake is important as potential dietary habits to prevent gout in Japanese people. The previous reports [36-40] showed modification of dietary habits for the prevention of gout in Japanese people through the trends in nutrient intakes of Japanese people in 1946-2022. This article suggests modification of micronutrient intake for the prevention of gout in Japanese people referencing the results of clinical research (clinical trials and epidemiological studies) through the results of relationship between the number of gout patients and micronutrient (vitamin, mineral, or salt) intake and evaluation of the daily dietary nutrient intake of Japanese people using

Dietary Reference Intakes definitions set by the Ministry of Health, Labour and Welfare (MHLW) in Japan [41] and the Institute of Medicine (IOM) of the National Academy of Sciences in the U.S. [42, 43].

2. Methods

2.1. The Number of Gout Patients

The number of gout patients was estimated in the Comprehensive Survey of Living Conditions performed by the Ministry of Health, Labour and Welfare (MHLW) in Japan (1986-2022) [33-35]. 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. The number of gout patients 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 [33-35]. 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 [35]. 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 [35]. Almost all gout patients were adults, and the number of gout patients was higher in men than in women.

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 MHLW in Japan [44-46]. Data were extracted from the series of Japanese National Nutrition Surveys that have been carried out every year throughout Japan since 1946 [45]. 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) [44, 46].

2.3. Dietary Reference Intakes for Japanese People

The MHLW in Japan [41] 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 the Institute of Medicine (IOM) of the National Academy of Sciences in the U.S. [42] 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 [47, 48] and the National Institutes of Health in the U.S. Department of Health & Human Services [49].

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

3.1. Relationship Between the Number of Gout Patients and Micronutrient Intake

The results on the correlation between the number of gout patients and intake of micronutrient or salt in Japanese people are shown in Tables 1 and 2. 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 1. *Correlation between number of gout patients and intake of micronutrient or salt in Japanese people in 1986-2019 and 1986-2022.*

Year	1986-2019	1986-2022
Micronutrient	coefficient	coefficient
Vitamins		
Vitamin A[†, ††]	- 0.893***	- 0.888***
Vitamin B_1[†, ††]	- 0.880***	- 0.832***
Vitamin B_2	- 0.756**	- 0.747**
Vitamin C	- 0.900***	- 0.894***
Minerals or salt		
Salt[†††††]	- 0.913***	- 0.926***
Calcium[†, ††]	- 0.757**	- 0.793**
Iron	- 0.894***	- 0.887***
	2001-2019	2001-2022
	coefficient	coefficient
Vitamins		
Vitamin D	- 0.891**	- 0.912**
Vitamin E[†, ††]	- 0.706	- 0.709*
Vitamin K	- 0.615	- 0.412
Niacin[†††]	0.677	0.793*
Pantothenic acid	- 0.138	0.112
Vitamin B_6	- 0.413	- 0.488
Folate[†, ††]	- 0.748	- 0.747*
Vitamin B_{12}[††††]	- 0.812*	- 0.873**
Minerals or salt		
Potassium[†, ††]	- 0.624	- 0.592
Magnesium[†, ††]	- 0.620	- 0.590
Phosphorus	- 0.554	- 0.440
Copper[†††]	- 0.852*	- 0.875**
Zinc[†]	- 0.304	- 0.138
	1995-2019	1995-2022
	coefficient	coefficient
Sodium	- 0.964***	- 0.959***

The Pearson Product Moment Correlation coefficient, * for P<0.05, ** for P<0.01, *** for P<0.001.
[†]The daily micronutrient intake of Japanese people (aged ≥ 15 years) in 2019 were below the Recommended Dietary Allowances (RDAs) or the Adequate Intakes (AIs). [††]The daily micronutrient intake of Japanese people (aged ≥ 15 years) in 2022 were below the Recommended Dietary Allowances (RDAs) or the Adequate Intakes (AIs). [†††]The daily copper intake of Japanese people (aged ≥ 15 years) in 2022 were above the Recommended Dietary Allowances (RDAs). [††††]The daily vitamin B_{12} intake of Japanese people (aged ≥ 15 years) in 2019 and 2022 were above the Recommended Dietary Allowances (RDAs). [†††††]The daily salt intake of Japanese people (aged ≥ 1 year) in 2019 and 2022 exceeded the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG).

Table 2. *Correlation between number of gout patients and intake of micronutrient or salt in Japanese adult population, adult men, and adult women in 2004-2022.*

Year	Adults	Adult men	Adult women
2004-2022		coefficient	
Micronutrient			
Vitamins			
Vitamin A[†]	- 0.604	- 0.644	0.730
Vitamin D	- 0.910**	- 0.926**	0.331
Vitamin E[†]	- 0.755**	- 0.740	0.626
Vitamin K	- 0.022	0.222	0.521
Vitamin B_1[†]	- 0.808*	- 0.768*	0.276
Vitamin B_2	- 0.822*	- 0.807*	0.295
Niacin[††]	0.833*	0.813*	- 0.094
Pantothenic acid	0.692	0.700	0.317
Vitamin B_6	- 0.842*	- 0.843*	0.273
Folate[†]	- 0.647	- 0.654	0.546
Vitamin B_{12}[††]	- 0.822*	- 0.826*	0.573
Vitamin C	- 0.857*	- 0.865*	0.507
Minerals or salt			
Salt[†††]	- 0.917**	- 0.942**	0.571
Calcium[†]	- 0.830*	- 0.792*	0.718

Year	Adults	Adult men	Adult women
Potassium†	- 0.291	- 0.352	0.680
Magnesium†	- 0.254	- 0.424	0.669
Phosphorus	0.119	- 0.042	0.603
Iron	- 0.755*	- 0.788*	0.564
Copper††	- 0.863*	- 0.927**	0.750
Zinc	0.325	0.050	0.425

The Pearson Product Moment Correlation coefficient, * for P<0.05, ** for P<0.01, *** for P<0.001.
†The daily micronutrient intake of Japanese people (aged ≥ 15 years) in 2022 were below the Recommended Dietary Allowances (RDAs) or the Adequate Intakes (AIs). ††The daily micronutrient intake of Japanese people (aged ≥ 15 years) in 2022 were above the Recommended Dietary Allowances (RDAs) or the Adequate Intakes (AIs). †††The daily salt intake of Japanese people (aged ≥ 1 year) in 2019 and 2022 exceeded the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DG).

3.1.1. Vitamins

Vitamin A

The daily vitamin A (retinol equivalent) intake of Japanese people in 2022 was higher compared to that in 1960, 1965, and 1975 and was lower compared to that in 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1960: 354.0 μgRAE; 1965: 397.2 μgRAE; 1975: 480.6 μgRAE; 1986: 650.7 μgRAE; 1989: 806.1 μgRAE; 1992: 794.7 μgRAE; 1995: 852.0 μgRAE; 1998: 810.3 μgRAE; 2001: 981.0 μgRAE; 2004: 879.0 μgRAE; 2007: 615.0 μgRAE; 2010: 529.0 μgRAE; 2013: 516.0 μgRAE; 2016: 524.0 μgRAE; 2019: 534.0 μgRAE; 2022: 515.0 μgRAE). The daily vitamin A intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.893, p= 0.0000933) and in 1986-2022 (r= -0.888, p= 0.0000493) (Table 1).

The daily vitamin A intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 547.0 μgRAE; 2022: 516.0 μgRAE). The intake of vitamin A did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.585, p=0.222) and in 2004-2022 (r= -0.604, p= 0.151)(Table 2). The daily vitamin A 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: 564.0 μgRAE; 2022: 538.0 μgRAE, women: 2019: 532.0 μgRAE; 2022: 497.0 μgRAE). The intake of vitamin A did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.636, p= 0.175) and in 2004-2022 (r= -0.644, p= 0.119) (Table 2). The intake of vitamin A tended to be positively correlated with number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.806, p= 0.0526) and in 2004-2022 (r= 0.730, p= 0.0626) (Table 2).

The daily vitamin A (retinol equivalent) intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 420-673 μgRAE/day and 402-612 μgRAE/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 800-900 μgRAE/day; women (aged ≥ 15 years): 650-700 μgRAE/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 900 μgRAE/day; women (aged ≥ 14 years): 700 μgRAE/day] [42].

Vitamin A, which is also called retinol, is a potent exogenous antioxidant for humans [10, 16, 50]. A cross-sectional study in Korea showed that subjects with hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women] had lower retinol intakes than controls [51]. Retinol intake was not significantly associated with SUA concentrations both in the Australian cohort and the Norwegian cohort [52].

A cross-sectional study survey using the National Health and Nutrition Examination Survey (NHANES) 2009-2014, the daily intake of total retinol and animal-derived retinol were inversely associated with hyperuricemia risk among U.S. adult men and women (aged ≥ 20 years) [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women] [26]. This article revealed that participants in the highest level of the daily intake of total retinol (≥ 861.00 RAE, mcg/day) and animal-derived retinol (≥ 371.50 RAE, mcg/day) were 29.0% and 24.0% less likely to be hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women] compared to those subjects in the lowest intake level of total retinol (< 283.50 RAE, mcg/day) and animal-derived retinol (< 98.00 RAE, mcg/day) [total retinol: OR = 0.71 (95% confidence interval, 0.520-0.960); animal-derived retinol: OR = 0.76 (95% confidence interval, 0.590-0.960)], respectively [26]. Though there was no significant association between plant-derived retinol intake and hyperuricemia risk in U.S. adult men and women (aged ≥ 20 years) [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women], participants in the highest level of the daily plant-derived retinol intake (≥ 544.50 RAE, mcg/day) were 8.0% less likely to be hyperuricemia compared to those subjects in the lowest intake level of plant-derived retinol (< 102.50 RAE, mcg/day) [OR = 0.92 (95% confidence interval, 0.720-1.170)] [26]. In a cross-sectional survey, retinol intake was not significantly associated with hyperuricemia risk [27]. The mechanism underlying the association between retinol intake and hyperuricemia remains poorly understood. However, Zhang et al. [26] have stated that retinol intake reduces oxidative stress and inflammatory response and further decreases UA synthesis, thereby providing a potential mechanism for retinol to reduce the risk of hyperuricemia.

Judging from the data of food composition [47-49], it is important for Japanese people (aged ≥ 14 years) to eat organ meats (liver, breast), seafood (salmon, tuna, herring, firefly squid, eel, conger eel, sablefish), potatoes, grains (fortified ready-to-eat cereals), nuts (pistachio nuts), legumes (black-eyed peas, baked beans), seaweed, fruit (apricots, mangos, cantaloupes), vegetables (spinach, carrots, peppers, broccoli, Jew's mallows, perillas), dairy products (milk, cheese, yogurt), eggs to take in more vitamin A to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42]. Serum vitamin A (retinol) levels were positively associated with SUA concentrations [53, 54] and hyperuricemia risk [53]. It seems that Japanese people (aged ≥ 20 years) need to decrease retinol intake or pay attention to not to excessive intake of retinol.

Vitamin D

The daily vitamin D of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (2001: 8.4 μg/day; 2004: 7.9 μg/day; 2007: 7.6 μg/day; 2010: 7.3 μg/day; 2013: 7.5 μg/day; 2016: 7.5 μg/day; 2019: 6.9 μg/day; 2022: 6.2 μg/day). The daily vitamin D intake was negatively correlated with the number of gout patients in 2001-2019 (r= -0.891, p= 0.00709) and in 2001-2022 (r= -0.912, p= 0.00161) (Table 1).

The daily vitamin D intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 7.2 μg/day; 2022: 6.5 μg/day). The intake of vitamin D was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.886, p= 0.0187) and in 2004-2022 (r= -0.910, p= 0.0044) (Table 2). The daily vitamin D 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: 7.9 μg/day; 2022: 7.1 μg/day, women: 2019: 6.6 μg/day; 2022: 6.1 μg/day). The intake of vitamin D was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.932, p= 0.00677) and in 2004-2022 (r= -0.926, p= 0.00278) (Table 2). The intake of vitamin D did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.684, p= 0.134) and in 2004-2022 (r= 0.331, p= 0.469) (Table 2). This result suggests that the correlation of daily vitamin D intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily vitamin D intake of Japanese men (aged 15-69 years) and women (aged ≥15 years) in 2022 were 5.0-7.5 μg/day and 4.0-7.7 μg/day, respectively, and were below the AIs established by the MHLW in Japan [men (aged 15-69 years): 8.5-9.0 µg/day; women (aged ≥ 15 years): 8.5 µg/day] [41]. The daily vitamin D intake of Japanese men (aged ≥ 70 years) in 2022 was 8.6-9.2 μg/day and was above the AIs established by the MHLW in Japan [men (aged ≥ 70 years): 8.5 μg/day] [41]. The AIs for vitamin D in the U.S. men and women (aged 0-50 years), men and women (aged 51-70 years), men and women (aged ≥ 71 years) established by the IOM of the National Academy of Sciences in the U.S. are 5 μg/day, 10 μg/day and 15 μg/day, respectively [42]. The daily vitamin D intake of Japanese men (aged 15-49 years) was 5.0-6.1 μg/day and was above the AIs established by the IOM of the National Academy of Sciences in the U.S. [men (aged 0-50 years): 5 μg/day] [42]. Whereas the daily vitamin D intake of Japanese men (aged ≥ 60 years) and Japanese women (aged ≥ 50 years) were 7.5-9.2 μg/day and 5.4-7.7 μg/day, respectively, and were below the AIs established by the IOM of the National Academy of Sciences in the U.S. [men (aged 51-70 years): 10.0 μg/day; men (aged > 70 years): 15.0 μg/day; women (aged 20-39 years): 5.0 μg/day; women (aged 50-69 years): 10.0 μg/day; women (aged ≥ 70 years): 10.0-15.0 μg/day] [42]. The RDAs for vitamin D in the U.S. men and women (aged 19-70 years), men and women (aged ≥ 71 years) established by the Food and Nutrition Board at IOM in the U.S. are 15 μg/day and 20 μg/day, respectively [55]. Though the daily vitamin D intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 15 years) in 2022 were 5.0-9.2 μg/day and 4.3-7.7 μg/day, respectively, the daily vitamin D intake of them were below the RDAs established by the Food and Nutrition Board at IOM in the U.S. [55].

Vitamin D and vitamin D receptor signaling together have a suppressive role on autoimmunity and an anti-inflammatory effect [29]. Vitamin D intake was inversely associated with hyperuricemia risk among U.S. adult participants in the NHANES 2007-2014 [30]. The average daily vitamin D intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 7.1 μg/day and 6.1 μg/day, respectively. From the results of this article, male subjects in the fourth level of vitamin D intake (4.6-7.6 μg/day) were 32% less likely to be hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 µmol/L) in males and ≥ 6.0 mg/dL (356.9 μmol/L) in females] compared to those subjects in the lowest intake level (< 1.1 μg/day). Female subjects in the fourth level of vitamin D intake (3.7-6.2 μg/day) were 19% less likely to be hyperuricemia compared to those subjects in the lowest intake level (< 0.9 μg/day) [30]. From the result of this article [30], it seems that Japanese adult population (aged ≥ 20 years) need to take in more vitamin D. In an analysis of the NHANES 2007-2014, serum 25-hydroxyvitamin D concentrations might be inversely associated with hyperuricemia risk in general U.S. adults (aged ≥ 18 years) [56]. Vitamin D deficiency was associated with hyperuricemia [57]. A review reported by Charoenngam [58] suggests that correcting vitamin D deficiency (serum 25-dihydroxyvitamin D concentration < 20 ng/mL) and insufficiency (serum 25-dihydroxyvitamin D concentration 20-< 30 ng/mL) has a mild uric acid (UA)-lowering effect (~0.3-0.6 mg/dL), which is thought to be mediated by the suppression of parathyroid hormone, which is known to downregulate the ATP-binding cassette transporter G2 (ABCG2) in the kidneys, leading to a reduction in the renal clearance of UA [59]. These reports suggest importance of vitamin intake to prevent hyperuricemia. Furthermore, serum

UA, CRP, and interleukin-22 (IL-22) levels were significantly higher in acute gouty arthritis patients than in healthy controls [31]. Whereas serum 1,25-dihydroxy vitamin D3 levels were significantly lower in acute gouty arthritis patients than in healthy controls [31]. These results indicate that vitamin D3 plays a protective role in gout.

Judging from the data of food composition [47-49] and roles in the body of vitamin D (promotion of calcium absorption, reduction of inflammation, modulation of such processes as cell growth, neuromuscular and immune function, and glucose metabolism) [49], it is important for Japanese men (aged ≥20 years) and Japanese women (aged ≥20 years) to eat meats (ground beef), organ meats (beef liver, chicken breast, monkfish liver), seafood (salmon, trout, swordfish, sturgeon, cisco, whitefish, mackerel, tuna, sardines, rockfish, tilapia, flatfish, bonito, dried whitebait, Japanese pilchard, herring, salmon roe, mullet roe, herring roe, anchovy, sand eel), fish oil (cod liver), grains (ready-to-eat cereal fortified with 10% Daily Value vitamin D, brown rice, whole wheat bread), legumes (lentils, edamame), seeds and nuts (almonds, sunflower seeds), mushrooms (wood ear, maitake mushrooms, shiitake mushrooms), milks (whole milk, whole chocolate milk, soy milk, almond milk), fruit (bananas, apples), vegetables (spinach, carrots, broccoli), dairy products (yogurt, cheese), eggs to take in more vitamin D to reach the RDAs set by the Food and Nutrition Board at IOM in the U.S. [men and women (aged 19-70 years): 15.0 μg/day; men and women (aged ≥ 71 years): 20 μg/day] [55]. However, it must be careful not to exceed the ULs of the daily vitamin D intake [men (aged ≥ 1 year): 50 μg/day; women (aged ≥ 1 year): 50 μg/day].

Vitamin E

The daily vitamin E intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, and 2010 and was higher compared to that in 2013, 2016, and 2019 (2001: 8.5 mg/day; 2004: 10.5 mg/day; 2007: 8.6 mg/day; 2010: 7.9 mg/day; 2013: 6.4 mg/day; 2016: 6.4 mg/day; 2019: 6.7 mg/day; 2022: 6.8 mg/day). The daily vitamin E intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.706, p= 0.0762) (Table 1). Whereas the daily vitamin E intake was negatively correlated with the number of gout patients in 2001-2022 (r= -0.709, p= 0.0491) (Table 1).

The daily vitamin E intake of Japanese adult population (aged ≥ 20 years) was higher compared to that in 2019 (2019: 6.9 mg/day; 2022: 7.0 mg/day). The daily vitamin E intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.773, p= 0.0712) (Table 2). Whereas the daily vitamin E intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022 (r= -0.755, p= 0.0050) (Table 2). The daily vitamin E intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 were the same as those in 2019, respectively (men: 2019: 7.2 mg/day; 2022: 7.2 mg/day; women: 2019: 6.6 mg/day; 2022: 6.6 mg/day). The daily vitamin E intake tended to be negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.793, p= 0.0600) and in 2004-2022 (r= -0.740, p= 0.0571) (Table 2). The daily vitamin E intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.703, p= 0.119) and in 2004-2022 (r= 0.626, p= 0.133) (Table 2).

The daily vitamin E intake of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 6.7-7.8 mg/day and 5.8-7.3 mg/day, respectively, and were above the AIs established by the MHLW in Japan [men (aged ≥ 15 years): 6.0-7.0 mg/day; women (aged ≥ 15 years): 5.0-6.5 mg/day], and were below the ULs established by the MHLW in Japan [men (aged ≥ 15 year): 750-900 mg/day; women (aged ≥ 15 year): 650-700 mg/day] [41]. The EARs and the RDAs for vitamin E in the U.S. men (aged ≥ 14 years) and women (aged ≥ 14 years) established by the IOM of the National Academy of Sciences in the U.S. are 12 mg/day and 15 mg/day, respectively [42]. In Dietary Reference Intakes for Japanese established by the MHLW in Japan, the daily vitamin E intake in Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) appears to be very unlikely to cause a deficiency. However, judging from Dietary Reference Intakes established by the IOM of the National Academy of Sciences in the U.S. [42], Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) need to take in more vitamin E to reach the RDAs.

Vitamin E suppressed the elevation of SUA concentrations and hypertension in deoxycorticosterone-salt-treated hypertensive rats via the uricosuric (increasing or promoting the excretion of UA in urine) effect [60]. The co-administration of ethanol and vitamin E suppressed the elevation of SUA concentrations induced by ethanol consumption in both men and women [61]. Vitamin E intake was not significantly associated with SUA concentrations both in the Australian cohort and the Norwegian cohort [52]. In the NHANES 2009-2014, dietary vitamin E intake was inversely associated with hyperuricemia risk in U.S. adult population (aged ≥ 20 years), especially among males and participants aged ≥ 60 years [17]. This article revealed that the risk of hyperuricemia reached a relatively low level when the dietary vitamin E intake was close to 10.0 mg/day [17]. The average daily vitamin E intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 7.3 mg/day and 6.6 mg/day, respectively. It seems that Japanese adult population (aged ≥ 20 years) need to take in 10.0 mg/day of vitamin E or the AIs set by the IOM of the National Academy in the U.S.

Vitamin E is a potent antioxidant [10]. Vitamin E protects cell membranes from oxidative damage by inhibiting free radical production and reducing oxidative stress [62]. He et al. [62] have stated that vitamin E may mitigate the negative impact of oxidative stress on UA metabolism, thereby lowering hyperuricemia risk. A possible mechanism of higher vitamin E intake associated with lower hyperuricemia risk could be that vitamin E inhibits the activity of xanthine oxidase [63] and has uricosuric (increasing or promoting the excretion of UA in urine) effect [60] and antioxidant activity [10, 62].

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) to eat organ meats (sweetfish liver, monkfish liver), seafood (salmon roe), wheat germ, seeds and nuts (sunflower seeds, almonds, hazelnuts, peanuts), vegetables (spinach, broccoli, tomatoes, chili pepper), and fruit (kiwifruit, mangos), eggs (egg yolk), fats and oils (peanut butter, margarine, wheat germ oil, sunflower oil, corn oil, soybean oil, rapeseed oil, mayonnaise, shortening), green tea and matcha, tea to take in more vitamin E to reach the RDAs established by the IOM of the National Academy of Sciences in the U.S..

Vitamin K

The daily vitamin K intake of Japanese people in 2022 was lower compared to that in 2001 and was higher compared to that in 2004, 2007, 2010, 2013, 2016, and 2019 (2001: 267 μg/day; 2004: 242 μg/day; 2007: 235 μg/day; 2010: 227 μg/day; 2013: 220 μg/day; 2016: 225 μg/day; 2019: 240 μg/day; 2022: 245 μg/day). The daily vitamin K intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.615, p=0.142) and in 2001-2022 (r= -0.412, p= 0.310) (Table 1).

The daily vitamin K intake of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 250 μg/day; 2022: 253 μg/day). The daily vitamin K intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.318, p= 0.540) and in 2004-2022 (r= -0.022, p= 0.963) (Table 2). The daily vitamin K 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: 258 μg/day; 2022: 264 μg/day, women: 2019: 243 μg/day; 2022: 244 μg/day). The daily vitamin K intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.162, p= 0.759) and in 2004-2022 (r= 0.222, p= 0.633) (Table 2). The daily vitamin K intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.505, p= 0.306) and in 2004-2022 (r= 0.521, p= 0.230) (Table 2).

The daily vitamin K intake of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 223-288 μg/day and 169-295 μg/day, respectively, and were above the AIs established by the MHLW in Japan [men (aged ≥ 15 years): 150-160 μg/day; women (aged ≥ 15 years): 150 μg/day] [41]. The AIs for vitamin K in the U.S. men (aged 14-18 years), men (aged ≥ 19 years), women (aged 14-18 years), and women (aged ≥ 19 years) established by the IOM of the National Academy of Sciences in the U.S. are 75 μg/day, 120 μg/day, 75 μg/day, and 90 μg/day, respectively [42]. This suggests that the daily vitamin K intake in Japanese men (aged ≥ 14 years) and women (aged ≥ 14 years) appears to be very unlikely to cause a deficiency.

Vitamin K-rich foods are meat (ground beef, chicken breast, chicken liver, ham), seafood (salmon, shrimp), seaweed (wakame, nori, hijiki), legumes (soybeans, edamame), soy products (natto), nuts (cashew nuts, pine nuts, mixed nuts), fruit (blueberries, grapes), vegetables (collards, turnip greens, spinach, kales, broccoli, carrots, Jew’s mallows, perillas, iceberg lettuces, pumpkins, okra, parsley), oil (soybean oil, olive oil, canola oil), dairy products (milk, cheddar cheese, mozzarella cheese), eggs, green tea and matcha, tea, carrot juice, vegetable juice [47-49]. It seems that Japanese people need to decrease vitamin K intake or pay attention to not to excessive intake of vitamin K.

Vitamin B_1

The daily vitamin B_1 intake of Japanese people in 2022 was lower compared to that in 1960, 1965, 1975, 1986, 1989, 1992, 1995, and 1998 and was higher compared to that in 2001, 2004, 2007, 2010, 2013, and 2016 and was the same as that in 2019 (1960: 1.05 mg/day; 1965: 0.97 mg/day; 1975: 1.11 mg/day; 1986: 1.35 mg/day; 1989: 1.23 mg/day; 1992: 1.25 mg/day; 1995: 1.22 mg/day; 1998: 1.16 mg/day; 2001: 0.89 mg/day; 2004: 0.86 mg/day; 2007: 0.87 mg/day; 2010: 0.83 mg/day; 2013: 0.80 mg/day; 2016: 0.86 mg/day; 2019: 0.95 mg/day; 2022: 0.95 mg/day). The daily vitamin B_1 intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.880, p= 0.000157) and in 1986-2022 (r= -0.832, p= 0.000042) (Table 1).

The daily vitamin B_1 intake of Japanese adult population (aged ≥ 20 years) in 2022 was the same as that in 2019 (2019: 0.95 mg/day; 2022: 0.95 mg/day). The daily vitamin B_1 intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.831, p= 0.0404) and in 2004-2022 (r= -0.808, p= 0.0279) (Table 2). The daily vitamin B_1 intake of Japanese adult men (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 1.03 mg/day; 2022: 1.05 mg/day). The daily vitamin B_1 intake tended to be negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.793, p= 0.0599) (Table 2). The daily vitamin B_1 intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= -0.768, p= 0.0435) (Table 2). Whereas the daily vitamin B_1 intake of Japanese adult women (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 0.88 mg/day; 2022: 0.87 mg/day). The daily vitamin B_1 intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.344, p= 0.505) and in 2004-2022 (r= 0.276, p= 0.550) (Table 2). This result suggests that the correlation of daily vitamin B_1 intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily vitamin B_1 intake of Japanese [men (aged 15-19 years) and women (aged ≥ 50 years) in 2022 were 1.31 mg/day and 0.81-0.91 mg/day, respectively, and the daily vitamin B_1 intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 0.98-1.31 mg/day and 0.79-0.93 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged 15-17 years): 1.5 mg/day; men (aged 18-49 years): 1.4 mg/day; men (aged 50-74 years): 1.3 mg/day; men (aged ≥ 75 years): 1.2 mg/day; women (aged 15-17 years): 1.2 mg/day; women (aged 18-74 years): 1.1 mg/day; women (aged ≥ 75 years): 0.9 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 1.2 mg/day; women (aged 14-18 years): 1.0 mg/day; women (aged ≥ 19 years): 1.1 mg/day] [42].

Increased vitamin B_1 intake was associated with decreased SUA concentrations in the Australian cohort [52]. In the NHANES 2017-2020, the daily vitamin B_1 intake was inversely associated with hyperuricemia risk among U.S. adult men (aged ≥ 20 years) but not in women (aged ≥ 20 years) [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women] [64]. The average daily vitamin B1 intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 1.05 mg/day and 0.87 mg/day, respectively. From the results of this article, men in the second level of vitamin B1 intake (0.94-1.24 mg/day) was 25% less likely to be hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men] compared to those subjects in the lowest intake level (< 0.94 mg/day) [64]. It seems that Japanese adult population (aged ≥ 20 years) need to take in more vitamin B_1 to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

Sadek et al. [65] found that thiamine reduced UA levels and ameliorated hepatic, renal dysfunction and dyslipidemia in diabetic rats. Vatsalya et al. [66] examined the effect of thiamine on SUA concentrations in alcohol use disorder (AUD) patients for three-weeks. This result revealed that dose of thiamine (200 mg/day) to alcohol use disorder (AUD) patients significantly decreased SUA concentrations at day 22 compared to the baseline [66]. They [66] also have stated that abstinence and treatment with thiamine could alleviate hyperuricemia in heavy drinkers with mild or no alcohol-associated liver disease (ALD).

Judging from the data of food composition [47-49], it is important for Japanese people (aged ≥ 15 years) to eat meats (beef steak, pork, chicken), seafood (mussels, trout, tuna, walleye pollock, eel), mushrooms (maitake mushrooms), grains (white rice, egg noodle, bread, corn, barley, macaroni, whole wheat, brown rice, oatmeal, breakfast cereals fortified with 100% Daily Value thiamin), seaweed (nori), seeds and nuts (sunflower seeds, sesame seeds, chia seeds, Brazil nuts, peanuts), legumes (black beans, soybeans), fruit (avocados, apples), vegetables (broccoli, parsley), dairy products (milk, yogurt, cheddar cheese), eggs, orange juice to take in more vitamin B_1 to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

Vitamin B_2

The daily vitamin B_2 intake of Japanese people in 2022 was higher compared to that in 1960, 1965, 1975, 2010, 2013, and 2016 and was lower compared to that in 1986, 1989, 1992, 1995, 1998, 2001, and 2019 and was the same as that in 2004 and 2007 (1960: 0.72 mg/day; 1965: 0.83 mg/day; 1975: 0.96 mg/day; 1986: 1.26 mg/day; 1989: 1.33 mg/day; 1992: 1.36 mg/day; 1995: 1.47 mg/day; 1998: 1.42 mg/day; 2001: 1.22 mg/day; 2004: 1.17 mg/day; 2007: 1.17 mg/day; 2010: 1.13 mg/day; 2013: 1.10 mg/day; 2016: 1.15 mg/day; 2019: 1.18 mg/day; 2022: 1.17 mg/day). The daily vitamin B_2 intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.756, p= 0.00447) and in 1986-2022 (r= -0.747, p= 0.00334) (Table 1).

The daily vitamin B_2 intake of Japanese adult population (aged ≥ 20 years) in 2022 was the same as that in 2019 (2019: 1.19 mg/day; 2022: 1.19 mg/day). The daily vitamin B_2 intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.846, p= 0.0339) and in 2004-2022 (r= -0.822, p= 0.0231) (Table 2). The daily vitamin B_2 intake of Japanese adult men (aged ≥ 20 years) and adult women (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 1.25 mg/day; 2022: 1.26 mg/day). The daily vitamin B_2 intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.844, p= 0.0470) and in 2004-2022 (r= -0.807, p= 0.0281) (Table 2). Whereas the daily vitamin B_2 intake of Japanese adult women (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 1.13 mg/day; 2022: 1.12 mg/day). The daily vitamin B_2 intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.370, p= 0.470) and in 2004-2022 (r= 0.295, p= 0.521) (Table 2). This result suggests that the correlation of daily vitamin B_2 intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily vitamin B_2 intake of Japanese men (aged 15-69 years) and women (aged 15-59 years) in 2022 were 1.13-1.35 mg/day and 0.92-1.12 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged 15-69 years): 1.30-1.70 mg/day; women (aged 15-59 years): 1.20-1.40 mg/day] [41]. The daily vitamin B_2 intake of Japanese men (aged 15-59 years) and women (aged 15-49 years) in 2022 were 1.13-1.29 mg/day and 0.92-1.01 mg/day, respectively, and were below the RDAs established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 1.30 mg/day; women (aged ≥ 14 years): 1.00-1.10 mg/day] [42]. The daily vitamin B_2 intake of Japanese men (aged ≥ 75 years) and women (aged ≥ 60 years) in 2022 were 1.34 mg/day and 1.18-1.23 mg/day, respectively, and were above the RDAs established by the MHLW in Japan [men (aged ≥ 75 years): 1.30 mg/day; women (aged ≥ 60 years): 1.0-1.2 mg/day] [41]. The daily vitamin B_2 intake of Japanese men (aged ≥ 60 years) and women (aged ≥ 50 years) in 2022 were 1.34-1.35 mg/day and 1.12-1.23 mg/day, respectively, and were above the RDAs established by the IOM of the

National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 1.30 mg/day; women (aged ≥ 19 years): 1.10 mg/day] [42]. Therefore, the daily vitamin B_2 intake of Japanese men (aged 15-59 years) and women (aged 15-49 years) in 2022 were below the RDAs, and those of Japanese men (aged ≥ 60 years) and women (aged ≥ 50 years) were above the RDAs established by the IOM of the National Academy of Sciences in the U.S. [42].

Higher vitamin B_2 intake was associated with lower SUA concentrations both in the Australian cohort and the Norwegian cohort [52]. Zykova et al. [52] found that the average reduction of SUA concentration was significant in most group when intakes were above 2 mg per day (the recommended daily dose is 1.3 mg for men and 1.1 mg for women). It is possible that vitamin B_2 intake prevent gout through a reduction of SUA concentrations.

Judging from the data of food composition [47-49], it is important for Japanese men (aged 15-59 years) and women (aged 15-49 years) to eat meats (beef steak, pigeon), organ meats (beef liver, chicken breast, pork liver, pork kidneys, chicken liver), seafood (clams, salmon, cod), mushrooms (maitake mushrooms, shiitake mushrooms), grains (white rice, egg noodle, bread, macaroni, whole wheat, brown rice, oats, breakfast cereals fortified with 100% Daily Value riboflavin), seeds and nuts (sunflower seeds, almonds), legumes (kidney beans), seaweed (nori, dried wakame), fruit (apples), vegetables (spinach, asparaguses, tomatoes, cauliflowers, chili pepper, parsley), soy products (miso), dairy products (milk, cheese, yogurt), eggs, green tea and matcha to take in more vitamin B_2 to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

Niacin (Vitamin B_3)

The daily intake of niacin equivalent (niacin) of Japanese people in 2022 was higher compared to that in 2001, 2004, 2007, 2010, 2013, and 2016 and was lower compared to that in 2019 (2001: 27.0 mg NE /day; 2004: 26.7 mg NE /day; 2007: 26.7 mg NE /day; 2010: 25.4 mg NE /day; 2013: 25.9 mg NE /day; 2016: 25.8 mg NE /day; 2019: 30.7 mg NE /day; 2022: 30.5 mg NE /day). The daily niacin intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= 0.677, p= 0.0946) (Table 1). Whereas the daily niacin intake was positively correlated with the number of gout patients in 2001-2022 (r= 0.793, p= 0.019) (Table 1).

The daily niacin intake of Japanese adult population (aged ≥ 20 years) was lower compared to that in 2019 (2019: 31.3 mg NE /day; 2022: 31.1 mg NE /day). The daily niacin intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r=0.725, p= 0.103) (Table 2). Whereas the daily niacin intake was positively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022 (r= 0.833, p= 0.020) (Table 2). The daily niacin 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 mg NE /day; 2022: 34.2 mg NE /day, women: 2019: 28.5 mg NE /day; 2022: 28.4 mg NE /day). The daily niacin intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r=0.702, p= 0.120) (Table 2). The daily niacin intake was positively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= 0.813, p= 0.0261) (Table 2). The daily niacin intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= -0.250, p= 0.633) and in 2004-2022 (r= -0.094, p= 0.841) (Table 2). This result suggests that the correlation of daily niacin intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily niacin intake of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 33.4-38.3 mg NE /day and 25.4-30.3 mg NE /day, respectively, and were above the RDAs [men (aged ≥ 15 year): 13.0-17.0 mg NE /day; women (aged ≥ 15 year): 10.0-13.0 mg NE /day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 year): 16.0 mg NE /day; women (aged ≥ 14 year): 14.0 mg NE /day] [42]. The daily niacin intake of Japanese men (aged 60-79 years) in 2022 were 35.0-35.1 mg NE /day and were above the ULs established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 19 years): 35.0 mg NE /day] [42]. It seems that the daily niacin intake of Japanese people except for men (aged 60-79 years) in 2022 appears to be very unlikely to cause a deficiency.

Niacin-rich foods are meat (beef, ground beef, tenderloin pork, chicken), organ meats (beef liver, smoked pork liver, chicken breast, turkey breast), seafood (salmon, tuna, cod roe, dried bonito, mackerel, bonito, sardines), grains (brown rice, breakfast cereals fortified with 25% Daily Value niacin, white rice, whole wheat bread, white bread), potatoes, seeds and nuts (peanuts, sunflower seeds, pumpkin seeds, cashew nuts), legumes (lentils, edamame, chickpeas), soy products (soymilk, tofu), mushrooms (maitake mushrooms, shiitake mushrooms), fruit (bananas, raisins, apples), vegetables (tomatoes, broccoli, onions, spinach), dairy products (milk, yogurt), eggs, coffee, marinara (spaghetti) sauce [47-49]. It seems that Japanese people need to decrease niacin intake.

Pantothenic Acid (Vitamin B_5)

The daily pantothenic acid intake of Japanese people in 2022 was lower compared to that in 2001 and was higher compared to that in 2004, 2007, 2010, 2013, 2016, and 2019 (2001: 5.71 mg/day; 2004: 5.52 mg/day; 2007: 5.46 mg/day; 2010: 5.24 mg/day; 2013: 5.41 mg/day; 2016: 5.45 mg/day; 2019: 5.65 mg/day; 2022: 5.66 mg/day). The daily pantothenic acid intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.138, p= 0.769) and in 2001-2022 (r= 0.112, p= 0.792) (Table 1).

The daily pantothenic acid intake of Japanese adult population (aged ≥ 20 years) in 2022 was higher compared to that in 2019 (2019: 5.65 mg/day; 2022: 5.67 mg/day). The daily pantothenic acid intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.533, p= 0.276) and in 2004-2022 (r= 0.692, p= 0.085) (Table 2). The daily pantothenic acid 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: 6.05 mg/day; 2022: 6.07 mg/day, women: 2019: 5.30 mg/day; 2022: 5.32 mg/day). The daily pantothenic acid intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= 0.546, p= 0.262) and in 2004-2022 (r= 0.700, p= 0.080) (Table 2). The daily pantothenic acid intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2 in 2004-2019 (r= 0.284, p= 0.585) and in 2004-2022 (r= 0.317, p= 0.488) (Table 2).

The daily pantothenic acid intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 50 years) in 2022 were 5.74-6.37 mg/day and 5.33-5.81 mg/day, respectively, and were above the AIs established by the MHLW in Japan [men (aged 20-49 years): 5.0 mg/day; men (aged ≥ 60 years): 6.0 mg/day; women (aged ≥ 18 years): 5.0 mg/day] [41]. The daily pantothenic acid intake of Japanese women (15-49 years) in 2022 was 4.59-4.97 mg/day and was below the AIs established by the MHLW in Japan [women (aged ≥ 18 years): 5.0 mg/day] [41]. However, the daily pantothenic acid intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 50 years) in 2022 were 5.74-6.93 mg/day and 5.33-5.81 mg/day, respectively, and were above the AIs established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 5.0 mg/day; women (aged ≥ 14 years): 5.0 mg/day] [42]. The daily pantothenic acid intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) were 6.07 mg/day and 5.32 mg/day, respectively, and were above the AIs established by the MHLW in Japan [men (aged ≥ 18 years): 5.0-6.0 mg/day; women (aged ≥ 18 years): 5.0 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 5.0 mg/day; women (aged ≥ 14 years): 5.0 mg/day] [42].

The daily pantothenic acid intake in Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) appears to be very unlikely to cause a deficiency. Pantothenic acid-rich foods are meats (beef, ground beef, poultry, sparrow, pigeon), organ meats (chicken breast, chicken liver, smoked pork liver, pork liver, beef kidney, pork kidney), seafood (tuna, eel, cod roe, sardines), mushrooms (shiitake mushrooms, maitake mushrooms), grains (breakfast cereals fortified with 100% Daily Value pantothenic acid, whole wheat, brown rice, oats), potatoes, nuts (peanuts), seeds (sunflower seeds), legumes (chickpeas), fruit (avocados, apples, clementine), vegetables (broccoli, carrots, cabbage, tomatoes), dairy products (milk, cheddar cheese, Greek yogurt), eggs, green tea and matcha [47-49]. Serum vitamin B5 (pantothenic acid) concentrations were positively associated with SUA concentrations [54]. It seems that Japanese people need to decrease pantothenic acid intake or pay attention to not to excessive intake of pantothenic acid.

Vitamin B_6

The daily vitamin B_6 intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, 2010, and 2019 and was higher compared to that in 2013 and 2016 (2001: 1.18 mg/day; 2004: 1.72 mg/day; 2007: 1.67 mg/day; 2010: 1.67 mg/day; 2013: 1.11 mg/day; 2016: 1.11 mg/day; 2019: 1.18 mg/day; 2022: 1.15 mg/day). The daily vitamin B_6 intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.413, p= 0.357) and in 2001-2022 (r= -0.488, p= 0.220) (Table 1).

The daily vitamin B_6 intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 1.20 mg/day; 2022: 1.18 mg/day). The daily vitamin B_6 intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.857, p= 0.0291) and in 2004-2022 (r= -0.842, p= 0.0174) (Table 2). The daily vitamin B_6 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: 1.30 mg/day; 2022: 1.27 mg/day, women: 2019: 1.12 mg/day; 2022: 1.09 mg/day). The daily vitamin B_6 intake was negatively correlated with number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.850, p= 0.0319) and in 2004-2022 (r= -0.843, p= 0.0173) (Table 2). Whereas the daily vitamin B_6 intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.349, p= 0.497) and in 2004-2022 (r= 0.273, p= 0.553) (Table 2). This result suggests that the correlation of daily vitamin B_6 intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily vitamin B_6 intake of Japanese men (aged ≥ 15 years) and women (aged 15-59 years) in 2022 were 1.14-1.39 mg/day and 0.92-1.08 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 1.40-1.50 mg/day; women (aged 15-59 years): 1.10-1.30 mg/day] [41]. The daily vitamin B_6 intake of Japanese women (aged ≥ 60 years) in 2022 was 1.15-1.23 mg/day and was above the RDAs established by the MHLW in Japan (1.10 mg/day) [41], but was below the RDAs established by the IOM of the National Academy of Sciences in the U.S. (1.50 mg/day) [42]. The RDAs for vitamin B_6 in the U.S. men (aged 14-50 years), men (aged ≥ 51 years), women (aged 14-50 years), and women (aged ≥ 51 years) are 1.3 mg/day, 1.7 mg/day, 1,2-1.3 mg/day, and 1.5 mg/day, respectively [42]. The daily vitamin B_6 intake of Japanese men (aged 20-49 years), men (aged ≥ 50 years), women (aged 20-49 years), and women (aged ≥ 50 years) in 2022 were 1.14-1.19 mg/day, 1.22-1.39 mg/day, 0.92-0.97 mg/day, and 1.08-1.23 mg/day, respectively. Therefore, the daily vitamin B_6 intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 15 years) were below the RDAs established by the IOM of the

National Academy of Sciences in the U.S. [42].

In the NHANES 2001-2014, no association between vitamin B_6 intake and hyperuricemia risk in both U.S. adult males and females (aged 20-85 years) [67].

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 20 years) and women (aged ≥ 15 years) to eat meats (turkey, chicken, pork fin), organ meats (chicken breast, beef liver, pork liver), seafood (tuna, salmon, skipjack, sardines, mackerel, Nile tilapia, squid), grains (white rice, buckwheat, fortified ready-to-eat cereals), potatoes, seeds and nuts (sunflower seeds, pistachio nuts, sesame seeds), legumes (chickpeas), seaweed, vegetables (onions, garlic, tomatoes, peppers), fruit (bananas, raisins, watermelons), dairy products (cheese), soy products (tofu) to take in more vitamin B_6 to reach the RDAs set by the IOM of the National Academy of Sciences in the U.S. [42]. However, it must be careful not to exceed the ULs of the daily vitamin B_6 intake.

Folate (Vitamin B_9)

The daily folate intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007 and 2019 and was higher compared to that in 2013 and 2016 and was the same as that in 2010 (2001: 313.0 μg/day; 2004: 294.0 μg/day; 2007: 299.0 μg/day; 2010: 281.0 μg/day; 2013: 280.0 μg/day; 2016: 277.0 μg/day; 2019: 289.0 μg/day; 2022: 281.0 μg/day). The daily folate intake tended to be negatively correlated with the number of gout patients in 2001-2019 (r= -0.748, p= 0.0532) (Table 1). Whereas the daily folate intake was negatively correlated with the number of gout patients in 2001-2022 (r= -0.747, p= 0.0333) (Table 1).

The daily folate intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 302.0 μg/day; 2022: 293.0 μg/day). The daily folate intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.594, p= 0.214) and in 2004-2022 (r= -0.647, p= 0.116) (Table 2). The daily folate 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: 310.0 μg/day; 2022: 302.0 μg/day, women: 2019: 295.0 μg/day; 2022: 285.0 μg/day). The daily folate intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.610, p= 0.199) and in 2004-2022 (r= -0.654, p= 0.111) (Table 2). The daily folate intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.642, p= 0.169) and in 2004-2022 (r= 0.546, p= 0.205) (Table 2).

The daily folate intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 40 years) in 2022 were 243.0-350.0 μg/day and 242.0-339.0 μg/day, respectively, and were above the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 240.0 μg/day; women (aged ≥ 15 years): 240.0 μg/day] [41]. The daily folate intake of Japanese women (aged 15-39 years) in 2022 was 207.0-220.0 μg/day and were below the RDAs established by the MHLW in Japan [women (aged ≥ 15 years): 240.0 μg/day] [41]. However, the daily folate intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 243-350 μg/day and 207-339 μg/day, respectively, and were below the RDAs established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years) and women (aged ≥ 14 years): 400 μg/day] [42].

Folic acid (84 μg/kg) and zinc (4 mg/kg) decreased SUA concentrations and serum adenosine deaminase and xanthine oxidase activities and enhanced the abundance of probiotics bacteria and reduced the abundance of pathogenic bacteria in high-purine diet-induced hyperuricemic rats [68]. These results suggest that folic acid and zinc ameliorate hyperuricemia by inhibiting UA biosynthesis and stimulating UA excretion by modulating the gut microbiota [68].

Increased folate intake was associated with decreased SUA concentrations in the Australian cohort [52] and the 2016-2019 Korea National Health and Nutrition Examination Survey [69]. On the other hand, long-term supplementation with folic acid had no effect on SUA concentrations in Norwegian patients with coronary artery disease [70].

Increased folate intake was associated with decreased hyperuricemia risk [67] and gout risk [71]. It is possible that folate intake prevent gout through a decrease in SUA concentrations.

In the NHANES 2001-2014, folate intake was inversely associated with hyperuricemia risk among U.S. adult males (aged 20-85 years), but no association between folate intake and hyperuricemia risk among U.S. adult females (aged 20-85 years) [67]. The average daily folate intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 302 μg/day and 285 μg/day, respectively. From the results of this article, male subjects in the second level of folate intake (248-347 μg/day) was 13% less likely to be hyperuricemia [SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in males] compared to those subjects in the lowest intake level (≤ 247 μg/day) [67]. Female subjects in the third level of folate intake (269-353 μg/day) was 18% less likely to be hyperuricemia [SUA concentration ≥ 6.0 mg/dL (356.9 μmol/L) in females] compared to those subjects in the lowest intake level (≤ 191 μg/day) [67]. From the result of this article [18], it seems that Japanese adult population (aged ≥ 20 years) need to take in more folate.

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) to eat meats (beef), organ meats (liver, breast), seafood (crab, halibut, sardines, sea urchin), mushrooms (maitake mushrooms, shiitake mushrooms), grains (white rice, spaghetti, bread, wheat, fortified ready-to-eat cereals), seeds and nuts (sunflower seeds, peanuts), legumes (black-eyed peas, kidney beans, green peas, soybeans, chickpeas), seaweed, fruit (avocados, oranges, papayas, bananas, mangos), vegetables (asparaguses, spinach, brussels sprouts, lettuces, broccoli, mustard greens, Jew's mallows), dairy products (milk), eggs, green tea to take in more folate to reach the RDAs established by the IOM of the National Academy of Sciences in the U.S. [42]. Serum vitamin B9 (folate) concentrations were positively associated with SUA concentrations [54]. It seems that Japanese people need to decrease folate intake or pay attention to not to excessive intake of folate.

Vitamin B_{12}

The daily vitamin B_{12} intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (2001: 7.7 μg/day; 2004: 7.0 μg/day; 2007: 7.1 μg/day; 2010: 6.0 μg/day; 2013: 6.1 μg/day; 2016: 6.0 μg/day; 2019: 6.3 μg/day; 2022: 5.4 μg/day). The daily vitamin B_{12} intake was negatively correlated with the number of gout patients in 2001-2019 (r= -0.812, p= 0.0264) and in 2001-2022 (r= -0.873, p= 0.0047) (Table 1).

The daily vitamin B_{12} intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 6.5 μg/day; 2022: 5.6 μg/day). The daily vitamin B_{12} intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.707, p= 0.116) (Table 2). Whereas the daily vitamin B_{12} intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022 (r= -0.822, p= 0.0231) (Table 2). The daily vitamin B_{12} 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: 7.3 μg/day; 2022: 6.3 μg/day, women: 2019: 5.9 μg/day; 2022: 5.1 μg/day). The daily vitamin B_{12} intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.723, p= 0.105) (Table 2). Whereas the daily vitamin B_{12} intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= -0.826, p= 0.0219) (Table 2). The daily vitamin B_{12} intake was positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.881, p= 0.0205) (Table 2). The daily vitamin B_{12} intake did not show a significant correlation with the number of gout patients n adult women (aged ≥ 20 years) in 2004-2022 (r= 0.573, p= 0.178) (Table 2). This result suggests that the correlation of daily vitamin B_{12} intake with the number of gout patients varies with gender and is stronger in adult women than in adult men.

The daily vitamin B_{12} intake for men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 4.4-7.2 μg/day and 3.5-6.2 μg/day, respectively, and were above the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 2.4 μg/day; women (aged ≥ 15 years): 2.4 μg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 2.4 μg/day; women (aged ≥ 14 years): 2.4 μg/day] [42]. The MHLW in Japan [41] and the IOM of the National Academy of Sciences in the U.S. [42] have not set the ULs for healthy people.

Long-term supplementation with vitamin B_{12} had no effect on SUA concentrations in Norwegian patients with coronary artery disease [70].

In the NHANES 2001-2014, vitamin B_{12} intake was inversely associated with hyperuricemia risk among U.S. adult males (aged 20-85 years), but no association between vitamin B_{12} intake and hyperuricemia risk among U.S. adult females (aged 20-85 years) [67]. The average daily vitamin B_{12} intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 6.3 μg/day and 5.1 μg/day, respectively. From the results of this article, male subjects in the fourth level of vitamin B_{12} intake (5.59-8.43 μg/day) was 21% less likely to be hyperuricemia [serum uric acid (SUA) concentration ≥ 7.0 mg/dL (416.4 μmol/L) in males] compared to those subjects in the lowest intake level (≤ 2.27 μg/day) [67]. Female subjects in the fourth level of vitamin B_{12} intake (3.92-5.93 μg/day) was 15% less likely to be hyperuricemia [serum uric acid (SUA) concentration ≥ 6.0 mg/dL (356.9 μmol/L) in females] compared to those subjects in the lowest intake level (≤ 1.56 μg/day) [67].

Further research is necessary to assess association between vitamin B_{12} intake and SUA concentrations or hyperuricemia risk. Harris et al. [72] have stated that vitamin B_{12} as drug associated with increased cellular turnover and destruction can lead to secondary hyperuricemia and gout.

Vitamin B_{12}-rich foods are meats (beef, ground beef), organ meats (beef liver, angler liver, pork liver, chicken liver, turkey breast, sweetfish liver, monkfish liver), seafood (clams, tuna, oysters, salmon, anchovy, freshwater, trout, lamprey eel, firefly squid, chub mackerel, salmon roe, sardines, mullet, sculpin), grains (bread, breakfast cereals fortified with 25% DV vitamin B_{12}), legumes and soybean processed foods (kidney beans, tempeh), seaweed (nori), fruit (bananas, strawberries), vegetables (spinach), dairy products (milk, yogurt, cheese), eggs [47-49]. It seems that Japanese people (aged ≥ 15 years) need to decrease vitamin B_{12} intake or pay attention to not to excessive intake of vitamin B_{12}.

Vitamin C

The vitamin C intake of Japanese people in 2022 was higher compared to that in 1960, 1965, 2010, and 2016 and was lower compared to that in 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2013, and 2019 (1960: 75.0 mg/day; 1965: 78.0 mg/day; 1975: 117.0 mg/day; 1986: 124.0 mg/day; 1989: 123.0 mg/day; 1992: 122.0 mg/day; 1995: 135.0 mg/day; 1998: 125.0 mg/day; 2001: 106.0 mg/day; 2004: 99.0 mg/day; 2007: 96.0 mg/day; 2010: 90.0 mg/day; 2013: 94.0 mg/day; 2016: 89.0 mg/day; 2019: 94.0 mg/day; 2022: 93.0 mg/day). The daily vitamin C intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.900, p= 0.0000661) and in 1986-2022 (r= -0.894, p= 0.0000376) (Table 1).

The daily vitamin C intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 99.0 mg/day; 2022: 98.0 mg/day). The daily vitamin C intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in

2004-2019 (r= -0.879, p= 0.0211) and in 2004-2022 (r= -0.857, p= 0.0137) (Table 2). The daily vitamin C 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: 96.0 mg/day; 2022: 95.0 mg/day, women: 2019: 101.0 mg/day; 2022: 100.0 mg/day). The daily vitamin C intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.873, p= 0.0233) and in 2004-2022 (r= -0.865, p= 0.0119) (Table 2). The daily intake of vitamin C did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.600, p= 0.208) and in 2004-2022 (r= 0.507, p= 0.246) (Table 2). This result suggests that the correlation of daily vitamin C intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily vitamin C intake of Japanese men (aged 15-59 years) and women (aged 15-59 years) in 2022 were 62.0-81.0 mg/day and 60.0-87.0 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged ≥ 12 years): 100.0 mg/day; women (aged ≥ 12 years): 100.0 mg/day] [41]. Whereas the daily vitamin C intake of Japanese men (aged ≥ 60 years) and women (aged ≥ 60 years) were 103-128 mg/day and 111-133 mg/day, respectively, and were above the RDAs established by the MHLW in Japan [men (aged ≥ 12 years): 100.0 mg/day; women (aged ≥ 12 years): 100.0 mg/day] [41]. The RDAs for vitamin C in the U.S. men (aged ≥ 19 years) and women (aged ≥ 19 years) established by the IOM of the National Academy of Sciences in the U.S. are 90.0 mg/day and 75.0 mg/day, respectively [42]. The daily vitamin C intake of Japanese men (aged 20-59 years) and women (aged 20-49 years) in 2022 were 62.0-81.0 mg/day and 60.0-68.0 mg/day, respectively, and were below the RDAs established by the IOM of the National Academy of Sciences in the U.S. [42]. Whereas the daily vitamin C intake of Japanese men (aged ≥ 60 years) and women (aged ≥ 50 years) in 2022 were 103.0-128.0 mg/day and 87.0-133.0 mg/day, respectively, and exceeded the RDAs established by the IOM of the National Academy of Sciences in the U.S. [42]. Therefore, the daily vitamin C intake of Japanese men (aged 20-59 years) and women (aged 20-49 years) in 2022 were below the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

In clinical trials, vitamin C decreased SUA concentrations [73-77]. Vitamin C intake was not significantly associated with SUA concentrations both in the Australian cohort and the Norwegian cohort [52]. On the other hand, increased intake of vitamin C was associated with decreased SUA concentrations [20, 23-25], hyperuricemia risk [23, 25, 27, 28], and gout risk [71, 78]. Vitamin C intake may prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

A possible mechanism of higher vitamin C intake associated with lower SUA concentration and reduced risk of hyperuricemia and gout are presumed to be due to the following four reasons: (1) vitamin C lowers SUA concentration through a uricosuric effect by competing with SUA on the urate transporter 1 (also known as solute carrier family 22, member 12, or SLC22A12) for re-absorption in the kidney proximal tubule [73. 75-77, 79]; (2) vitamin C inhibits the pro-oxidant actions of UA during copper-mediated low density lipoprotein cholesterol (LDL-cholesterol) oxidation, and could reduce oxidative stress and inflammation, and may be related to lower UA production [10]; (3) vitamin C, which exerts as an antioxidant, reduced uric acid-induced inflammation by inhibiting activation of responsible nucleotide-binding and oligomerization domain-like receptor, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome in monosodium urate (MSU)-induced inflammation [80];(4) a higher serum vitamin C level has a positive effect on purine metabolism and favors the reduction of UA level, thus reducing the risk of monosodium urate crystal deposition in joints structures and soft tissue [18]. The role of vitamin C in prophylaxis and treatment of gout including molecular role of vitamin C in the transport of UA in the proximal renal tubules and in inflammatory process regulation was reviewed in detail by Brzezińska et al. [18].

Choi et al. [78] found that vitamin C intake associated with lower gout risk have been approximately 500 mg/day or higher compared with vitamin C intake < 250 mg/day. UK Gout Society [81] has stated that taking additional vitamin C as a dietary supplement (500 to 1500 mg/day) can reduce blood UA levels.

Judging from the data of food composition [47-49], it is important for Japanese men (aged 20-59 years) and women (aged 20-49 years) to eat potatoes, legumes (green peas), seaweed (nori), fruit (oranges, grapefruit, cantaloupes, acerolas, guavas, yuzu, kiwifruit, lemons, strawberries, papayas, blackcurrants), vegetables (red pepper, green pepper, kales, peppers, parsley, broccoli, tomatoes, cauliflowers, peas, eggplants, brussels sprouts, Chinese cabbages, cabbages, mustard spinach, chili pepper, ginger), orange juice, tomato juice, acerola juice, green tea to take in more vitamin C to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

3.1.2. Minerals

Sodium and Salt

Sodium

The daily sodium intake of Japanese people in 2022 was lower compared to that in 1995, 1998, 2000, 2002, 2005, 2007, 2010, 2013, 2016, and 2019 (1995: 5.18 g/day; 1998: 5.00 g/day; 2000: 4.85 g/day; 2002: 4.48 g/day; 2005: 4.32 g/day; 2007: 4.18 g/day; 2010: 4.00 g/day; 2013: 3.87 g/day; 2016: 3.77 g/day; 2019: 3.83 g/day; 2022: 3.71 g/day). The daily sodium intake was negatively correlated with the number of gout patients in 1995-2019 (r= -0.964, p= 0.000474) and in 1995-2022 (r= -0.959, p= 0.000166) (Table 1).

The daily sodium intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2016: 2019: 3.96 g/day; 2022: 3.81 g/day). The daily sodium 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: 4.31 g/day; 2022: 4.15 g/day, women: 2019: 3.65 g/day; 2022: 3.53 g/day).

The Joint WHO/FAO Expert Consultation [82] has stated that the recommended intake of sodium is < 2 g/day. The daily sodium intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 3905-4363 mg/day and 3100-3789 mg/day, respectively, and exceeded the EARs established by the MHLW in Japan [men (aged ≥ 18 years): 600 mg/day; women (aged ≥ 18 years): 600 mg/day] [41]. On the other hand, the MHLW in Japan [41] have not set the AIs and the IOM of the National Academy of Sciences in the U.S. [42] and the IOM of the National Academies of Sciences, Engineering, and Medicine in the U.S. [43] have not set the EARs and the RDAs. The AIs and the ULs for sodium in the U.S. people (aged ≥ 14 years) established by the IOM in the U.S. are 1500 mg/day and 2300 mg/day, respectively [42, 43]. U.S. Department of Agriculture and U.S. Department of Health and Human Services [83] have stated that the daily sodium intake of Americans should be less than 2300 mg/day and even less for children younger than age 14. The daily sodium intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were above the ULs established by the IOM in the U.S. [42, 43]. It seems that the daily sodium intake of Japanese men and women in 2022 is excessive.

Sodium-rich foods are seafood (salted fish, anchovies canned, Alaska pollock, Pacific cod, salted shrimp), seaweed (dried wakame, kelp), soy products (miso, soy sauce), Chinese soup stock, bouillon, kelp tea [48].

Salt

The daily salt intake of Japanese people in 2022 was lower compared to that in 1975, 1980, 1985, 1986, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1975: 13.5 g/day; 1980: 12.9 g/day; 1985: 12.1 g/day; 1986: 12.1 g/day; 1995: 13.2 g/day; 1998: 12.7 g/day; 2001: 11.5 g/day; 2004: 10.7 g/day; 2007: 10.6 g/day; 2010: 10.2 g/day; 2013: 9.8 g/day; 2016: 9.6 g/day; 2019: 9.7 g/day; 2022: 9.4 g/day). The daily salt intake was negatively correlated with number of gout patients in 1986-2019 (r= -0.913, p= 0.0000331) and in 1986-2022 (r= -0.926, p= 0.00000057) (Table 1).

The daily salt intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 10.1 g/day; 2022: 9.7 g/day). The daily salt intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.884, p= 0.0195) and in 2004-2022 (r= -0.917, p= 0.0037) (Table 2). The daily salt 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: 10.9 g/day; 2022: 10.5 g/day, women: 2019: 9.3 g/day; 2022: 9.0 g/day). The daily salt intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.916, p= 0.0102) and in 2004-2022 (r= -0.942, p= 0.0015) (Table 2). The daily salt intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.749, p= 0.0864) and in 2004-2022 (r= 0.571, p= 0.181) (Table 2). This result suggests that the correlation of daily salt intake with the number of gout patients tends to vary with gender and is stronger in adult men than in adult women.

The daily salt intake of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 9.9-11.1 g/day and 7.9-9.6 g/day, respectively, and exceeded the Tentative Dietary Goal for Preventing Lifestyle-related Diseases (DGs) established by the MHLW in Japan [men (aged ≥ 15 year): < 7.5 g/day; women (aged ≥ 15 year): < 6.5 g/day] [41]. It is speculated that a decrease in daily salt intake in the situation of exceeding the DGs is associated with the number of patients with gout. Thus, it is important for Japanese people to reduce salt intake.

In an interventional trial of 90 subjects (aged 18-65 years) on a normal diet for 3 days at baseline, a low-salt diet for 7 days (3.0 g/day, NaCl), and a high-salt diet for an additional 7 days (18.0 g/day, NaCl), plasma UA levels increased from baseline to low-salt diet and decreased from low-salt diet to high-salt diet and the 24 h urinary sodium excretions showed inverse correlation with plasma UA and positive correlation with urinary UA excretions [84].

The guidelines for management of gout established by 2012 American College of Rheumatology [5] recommended the limit intake of salt in gout patients. The World Health Organization [85] has stated that keep salt intake to less than 5 g/day.

Calcium

The calcium intake of Japanese people in 2022 was higher compared to that in 1960 and 1965 and was lower compared to that in 1975, 1986, 1989, 1992, 1995, 1998, 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (1960: 389.0 mg/day; 1965: 465.0 mg/day; 1975: 550.0 mg/day; 1986: 551.0 mg/day; 1989: 540.0 mg/day; 1992: 539.0 mg/day; 1995: 585.0 mg/day; 1998: 568.0 mg/day; 2001: 550.0 mg/day; 2004: 538.0 mg/day; 2007: 531.0 mg/day; 2010: 510.0 mg/day; 2013: 504.0 mg/day; 2016: 502.0 mg/day; 2019: 505.0 mg/day; 2022: 500.0 mg/day). The daily calcium intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.757, p= 0.00435) and in 1986-2022 (r= -0.793, p= 0.00123) (Table 1).

The daily calcium intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 498.0 mg/day; 2022: 495.0 mg/day). The daily calcium intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.883, p= 0.0396) and in 2004-2022 (r= -0.830, p= 0.0207) (Table 2). The daily calcium 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: 503.0 mg/day; 2022: 501.0 mg/day, women: 2019: 494.0 mg/day; 2022: 491.0 mg/day). The daily calcium intake tended to be negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.781, p= 0.0668) (Table 2). The daily calcium intake was negatively correlated with the number of gout patients in the adult men (aged ≥ 20 years) in 2004-2022 (r= -0.792, p= 0.0338) (Table 2). Whereas the daily calcium intake tended to be positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.786, p= 0.0639) and in 2004-2022 (r= 0.718, p=0.0693) (Table 2). This result suggests that the correlation of daily calcium intake with the number of gout patients tends to vary with gender.

The daily calcium intake of Japanese men (aged ≥ 15 year) and women (aged ≥ 15 year) in 2022 were 419-588 mg/day and 359-572 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 700-800 mg/day; women (aged ≥ 15 years): 600-650 mg/day] [41] and the AIs established by the IOM of the National Academy of Sciences in the U.S. [men and women (aged 14-18 years): 1300 mg/day; men and women (aged 19-50 years): 1000 mg/day; men and women (aged ≥ 51 years): 1200 mg/day] [42]. It seems that Japanese population (aged ≥ 15 years) need to take in more calcium.

A randomized, placebo controlled clinical trial showed that a difference of calcium intake of 1200 mg per day was associated with a difference in SUA levels of 0.022 mmol/L [86]. In epidemiological studies, increased intake of calcium was associated with decreased SUA concentrations [52. 68, 87] and hyperuricemia risk [27]. Zykova et al. [52] found that the minimal intake associated with statistically significant SUA concentration reduction was at level of approximately 1000 mg of calcium per day for men and 650 mg per day for women. It is possible that calcium intake prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

In a mendelian randomization study, blood calcium concentration had no association with gout risk [88].

Judging from the data of food composition [47-49], it is important for Japanese people (aged ≥ 15 years) to eat meats (sparrow), seafood (sardines, salmon, dried shrimp, dried flying fish, snails, crucian, carp, goby, loach), grains (breakfast cereals fortified with 10% Daily Value calcium, bread, tortillas), seeds and nuts (chia seeds, sesame seeds), potatoes (konjac), seaweed (hijiki, dried wakame), milks (almond milk, low-fat milk, skim milk, whole butter milk, whole chocolate milk), legumes (soybeans, beans, peas), fruit (apples), vegetables (spinach, okra, curly kale, Chinese cabbages, broccoli, parsley), dairy products (milk, cheese, yogurt, sour cream), soy products (soy milk, tofu), orange juice, to take in more calcium to reach the RDAs established by the MHLW in Japan [41] and the AIs established by the IOM of the National Academy of Sciences in the U.S..

Potassium

The daily potassium intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, and 2019 and was higher compared to that in 2010, 2013, and 2016 (2001: 2434 mg/day; 2004: 2321mg/day; 2007: 2306 mg/day; 2010: 2200 mg/day; 2013: 2231 mg/day; 2016: 2219 mg/day; 2019: 2299 mg/day; 2022: 2256 mg/day). The daily potassium intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.624, p= 0.134) and in 2001-2022 (r= -0.592, p= 0.122) (Table 1).

The daily potassium intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 2350 mg/day; 2022: 2305 mg/day). The daily potassium intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.268, p= 0.608) and in 2004-2022 (r= -0.291, p= 0.527) (Table 2). The daily potassium 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: 2439 mg/day; 2022: 2392 mg/day, women: 2019: 2273 mg/day; 2022: 2230 mg/day). The daily potassium intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.326, p= 0.529) and in 2004-2022 (r= -0.352, p= 0.438) (Table 2). The daily potassium intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.709, p= 0.115) and in 2004-2022 (r= 0.680, p= 0.093) (Table 2).

The daily potassium intake of Japanese men (aged 15-59 years) and women (aged 15-49 years) in 2022 were 2093-2297 mg/day and 1689-1932 mg/day, respectively, and were below the AIs established by the MHLW in Japan [men (aged 15-59 years): 2500-2700 mg/day; women (aged 20-39 years): 2000 mg/day] [41]. Whereas the daily potassium intake of Japanese men (aged ≥ 60years) and women (aged ≥ 50 years) in 2022 were 2532-2644 mg/day and 2174-2569 mg/day, respectively, and were above the AIs established by the MHLW in Japan [men (aged ≥ 60 years): 2500 mg/day; women (aged ≥ 40 years): 2000 mg/day] [41]. The daily potassium intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 2059-2644 mg/day and 1689-2569 mg/day, respectively, and were below the DGs established by the MHLW in Japan [men (aged ≥ 15 years): ≥ 3000 mg/day; women (aged ≥ 15 years): ≥ 2600 mg/day] [41] and were below the AIs established by the IOM of the National Academies of Sciences, Engineering, and Medicine in the U.S. [men (aged 14-18 years): 3000 mg/day; men (aged ≥ 19 years): 3400 mg/day; women (aged 14-18 years): 2300 mg/day; women (aged ≥ 19 years): 2600 mg/day] [43]. It seems that Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) need to take in more potassium.

In three cross-sectional studies in adult individuals, increased potassium intake was associated with increased urinary uric acid (UUA) excretion, thus potentially protecting against hyperuricemia [89]. The daily potassium intake of participants in these cohort studies were 3389 mg/d, 3002 mg/d, and 2955 mg/d, respectively, and the daily potassium intake of men was below the AIs established by the IOM of the National Academies of Sciences, Engineering, and Medicine in the U.S. [men (aged ≥ 19 years): 3400 mg/day; women (aged ≥ 19 years): 2600 mg/day] [43].

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) to eat meats (beef), organ meats (turkey breast, chicken breast), seafood (salmon, tuna), grains (brown rice, bread, white rice), potatoes (potato, konjac), legumes (kidney beans, soybeans, lentils), seeds and nuts (cashew nuts, flaxseed), seaweed (kelp, dried wakame, hijiki, nori), mushrooms (maitake mushrooms), fruit (banana, apricots, cantaloupe, prunes, raisins, apples), vegetables (squash, tomatoes, spinach, asparaguses, lettuces, broccoli, parsley, chili pepper), dairy products (milk, yogurt, mozzarella cheese), fats and oils (peanut butter, olive oil, corn oil, canola oil, soybean oil), eggs, soymilk, black tea, coffee, green tea and matcha, cocoa, orange juice to take in more potassium to reach the DG established by the MHLW in Japan [41] and the AIs established by the IOM of the National Academies of Sciences, Engineering, and Medicine in the U.S. [43]. It is encouraged to replace meat with fish and legumes.

Magnesium

The daily magnesium intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, and 2019 and was higher compared to that in 2010, 2013, and 2016 (2001: 262 mg/day; 2004: 250 mg/day; 2007: 247 mg/day; 2010: 236 mg/day; 2013: 239 mg/day; 2016: 238 mg/day; 2019: 247 mg/day; 2022: 242 mg/day). The daily magnesium intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.620, p= 0.137) and 2001-2022 (r= -0.590, p= 0.124) (Table 1).

The daily magnesium intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 255 mg/day; 2022: 250 mg/day). The daily magnesium intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.259, p= 0.620) and in 2004-2022 (r= -0.254, p= 0.582) (Table 2). The daily magnesium 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: 270 mg/day; 2022: 263 mg/day, women: 2019: 242 mg/day; 2022: 238 mg/day). The daily magnesium intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.315, p= 0.495) and in 2004-2022 (r= -0.424, p= 0.343) (Table 2). The daily magnesium intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.677, p= 0.140) and in 2004-2022 (r= 0.669, p= 0.100) (Table 2).

The daily magnesium intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 224-287 mg/day and 180-270 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged ≥ 15 years): 320-370 mg/day; women (aged ≥ 15 years): 260-310 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 400-420 mg/day; women (aged ≥ 14 years): 310-360 mg/day] [42]. It seems that Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) need to take in more magnesium.

A meta-analysis and systematic review reported that dietary magnesium intake was inversely associated with serum C-reactive protein (CRP) levels as biomarker of inflammation [90]. SUA level is positively associated with several inflammatory markers (e.g., white blood cell count, CRP, interleukin-6) [4]. This fact suggests that UA may have a role in inflammation and subsequent inflammatory related disease, such as gout. In an epidemiological study, increased magnesium intake was associated with decreased SUA concentrations [91] and hyperuricemia risk [91. 92]. Increased magnesium intake was significantly associated with decreased risk of hyperuricemia [SUA concentration ≥ 7.0 mg/ dL (416.4 μmol/L) in males and ≥ 6.0 mg/dL (356.9 μmol/L) in females] by analyses of the U.S. NHANES (2001-2014) databases involving 26,796 adults (aged 20-85 years) [92]. The average daily magnesium intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 263 mg/day and 238 mg/day, respectively. From the results of this article, male subjects in the second level of magnesium intake (200-265 mg/day) were 17% less likely to be hyperuricemia compared to those subjects in the lowest intake level (< 200 mg/day). Female subjects in the third level of magnesium intake (208-260 mg/day) were 14% less likely to be hyperuricemia compared to those subjects in the lowest intake level (< 158 mg/day) [92]. It seems that Japanese adult population (aged ≥ 20 years) need to take in ≥ 433 mg/day in men and ≥ 337 mg/day in women of magnesium or the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42]. It is possible that magnesium intake prevent gout through reduced SUA concentrations and decreased hyperuricemia risk.

In a mendelian randomization study, blood magnesium concentration was inversely associated with gout risk (OR = 0.26, 95% CI = 0.09, 0.76, p = 0.013); that is to say, each 0.16 mmol/L increase in genetically predicted magnesium was associated with a 0.26-fold increased risk of gout [88].

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) to eat meats (beef), organ meats (chicken breast), seafood (salmon, sardines), seeds and nuts (pumpkin seeds, chia seeds, sunflower seeds, almonds, peanuts, cashew nuts, sesame seeds, flaxseeds), grains (white rice, bread, brown rice, cereals, fortified ready-to-eat cereals, whole-wheat bread, oatmeal), potatoes, legumes (black beans, kidney beans, edamame), seaweeds, fruit (bananas, raisins, avocados, apples), vegetables (spinach, broccoli, carrots, parsley), dairy products (milk, yogurt), soy products (soy milk), tea, green tea to take in more magnesium to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

Phosphorus

The daily phosphorus intake of Japanese people in 2022 was lower compared to that in 2001, 2004, and 2019 and was higher compared to that in 2007, 2010, 2013, and 2016 (2001: 1057 mg/day; 2004: 1013 mg/day; 2007: 1000 mg/day; 2010: 960 mg/day; 2013: 978 mg/day; 2016: 976 mg/day; 2019: 1007 mg/day; 2022: 1001 mg/day). The daily phosphorus intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.554, p= 0.197) and in 2001-2022 (r= -0.440, p= 0.275) (Table 1).

The daily phosphorus intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 1012 mg/day; 2022: 1006 mg/day). The daily phosphorus intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.0215, p=0.968) and in 2004-2022 (r= 0.119, p= 0.799) (Table 2). The daily phosphorus 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: 1084 mg/day; 2022: 1076 mg/day, women: 2019: 948 mg/day; 2022: 946 mg/day). The daily phosphorus intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.151, p= 0.775) and in 2004-2022 (r= -0.042, p= 0.929) (Table 2). The daily phosphorus intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.593, p= 0.215) and in 2004-2022 (r= 0.603, p= 0.152) (Table 2).

The daily phosphorus intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 1006-1128 mg/day and 810-1031mg/day, respectively, and were above the AIs [men (aged ≥ 20 years): 1000 mg/day; women (aged ≥ 20 years): 800 mg/day] and were below the ULs established by the MHLW in Japan [men (aged ≥ 20 years): 3000 mg/day; women (aged ≥ 20 years): 3000 mg/day] [41]. The daily phosphorus intake of Japanese men (aged ≥ 20 years) and Japanese women (aged ≥ 20 years) in 2022 were above the RDAs for phosphorus established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 19 years): 700 mg/day; women (aged ≥ 19 years): 700 mg/day] [42]. It seems that Japanese adult population (aged ≥ 20 years) need to decrease intake of phosphorus to reach the AIs established by the MHLW in Japan [41] and the RDAs established by the IOM of the National Academy of Sciences in the U.S. [42]/

Phosphorus-rich foods are meats (beef), organ meats (chicken breast), seafood (salmon, scallops, flying fish, sardines, silver-striped herring, mackerel, dried bonito, dried shrimp, dried squid, dried baby sardines), grains (brown rice, oatmeal, bread, tortillas), potatoes, legumes (lentils, kidney beans, peas), seeds and nuts (cashew nuts, sesame seeds, chia seeds, pumpkin seeds, sunflower seeds), fruit (apples, clementine), vegetables (asparaguses, tomatoes, cauliflowers), dairy products (low-fat yogurt, milk, cheese), soy products (tofu), eggs, green tea, carbonated cola [47-49]. It seems that Japanese people (aged ≥ 20 years) need to decrease phosphorus intake or pay attention to not to excessive intake of phosphorus.

Iron

The daily iron intake of Japanese in 2022 was lower compared to that in 1960, 1975, 1980, 1986, 1995, 1998, 2001, 2004, 2007, 2010, and 2019 and was higher compared to that in 2013 and 2016 (1960: 13.0 mg/day; 1975: 13.4 mg/day; 1980: 10.4 mg/day; 1986: 10.7 mg/day; 1995: 11.8 mg/day; 1998: 11.4 mg/day; 2001: 8.2 mg/day; 2004: 7.9 mg/day; 2007: 7.9 mg/day; 2010: 7.6 mg/day; 2013: 7.4 mg/day; 2016: 7.4 mg/day; 2019: 7.6 mg/day; 2022: 7.5 mg/day). The daily iron intake was negatively correlated with the number of gout patients in 1986-2019 (r= -0.894, p= 0.000054) and in 1986-2022 (r= -0.887, p= 0.000088) (Table 1).

The daily iron intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 7.9 mg/day; 2022: 7.7 mg/day). The daily iron intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.718, p= 0.108) (Table 2). Whereas the daily iron intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2022 (r= -0.755, p= 0.0497) (Table 2). The daily iron 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: 8.3 mg/day; 2022: 8.1 mg/day, women: 2019: 7.5 mg/day; 2022: 7.4 mg/day). The daily iron intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.721, p= 0.106) (Table 2). Whereas the daily iron intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2022 (r= -0.788, p= 0.0353) (Table 2). The daily iron intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.623, p= 0.186) and in 2004-2022 (r= 0.564, p= 0.187) (Table 2). This result suggests that the correlation of daily iron intake with number of gout patients varies with gender and is stronger in adult men than in adult women.

The daily iron intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 year) in 2022 was 6.9-8.8 mg/day and 5.9-8.3 mg/day, respectively, and were above the EARs established by the MHLW in Japan [men (aged ≥ 20 years): 6.0-6.5 mg/day; women (aged ≥ 20 year): 5.0-5.5 mg/day] [41]. The daily iron intake of Japanese men (aged 20-29 years, aged 40-49 years) in 2022 were 6.9 mg/day and 7.2 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [men (aged 20-49 years): 7.5 mg/day] [10]. Whereas the daily iron intake of Japanese men (aged 30-39 years, aged ≥ 50 years) in 2022 were 7.7 mg/day and 7.9-8.8 mg/day, respectively, and were above the RDAs established by the MHLW in Japan [men (aged ≥ 18 years): 7.5 mg/day] [41]. In women, women with menstruation were evaluated by

Dietary Reference Intakes values established by the MHLW in Japan. The daily iron intake of Japanese women (aged 15-59 years) in 2022 were 5.9-7.2 mg/day, respectively, and were below the RDAs established by the MHLW in Japan [women with menstruation (aged 15-49 years): 10.5 mg/day; women with menstruation (aged 50-64 years): 11.0 mg/day] [41]. Whereas the daily iron intake of Japanese women (aged ≥ 65 years) in 2022 were 7.8-8.3 mg/day and were above the RDAs established by the MHLW in Japan [women (aged ≥ 65 years): 6.0 mg/day] and was below the ULs [men (aged ≥ 40 years): 40.0 mg/day] [41]. The daily iron intake of Japanese men (aged 20-59 years) and women (aged 20-69 years, ≥ 75 years) in 2022 were 6.9-7.9 mg/day and 5.9-7.9 mg/day, and 7.8 mg/day, respectively, and were below the RDAs established by the IOM of the National Academy of Sciences in the U.S. [men (aged 14-18 years): 11 mg/day; men (aged ≥ 15 years): 8 mg/day; women (aged 14-18 years): 15 mg/day; women (aged 19-50 years): 18 mg/day; women (aged ≥ 51 years): 8 mg/day] [42]. Whereas the daily iron intake for men (aged ≥ 60 years) and women (aged 70-79 years) were 8.7-8.8 mg/day and 8.3 mg/day, respectively, and exceeded the RDAs and was below the ULs established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 45.0 mg/day; women (aged ≥ 14 years): 45.0 mg/day] [42]. Increased iron intake was associated with decreased SUA concentrations in the Australian cohort [52]. Serum iron concentrations showed a positive correlation with SUA concentrations and the prevalence of hyperuricemia among 2824 subjects (mean age 52.2 ± 7.2) [hyperuricemia: SUA concentration ≥ 7.0 mg/dL (416.4 μmol/L) in men and ≥ 6.0 mg/dL (356.9 μmol/L) in women]; that is to say, subjects in the second level, the third level, the highest level of serum iron concentrations were 33%, 17%, 56% more likely to be hyperuricemia, compared to those subjects in the lowest intake level, respectively [93]. Iron is pro-oxidants [62], but metalloenzymes of catalase [22]. It is possible that iron intake prevent gout through a reduction of SUA concentrations and hyperuricemia risk. In a mendelian randomization study, blood iron concentration was inversely associated with gout risk (OR = 0.71, 95% CI = 0.53, 095, p = 0.047); that is to say, each per-unit increase in genetically predicted iron was associated with a 0.71-fold increased risk of gout [88].

From the data of food composition [47-49], it is important for Japanese men (aged 20-59 years) and women (aged 20-69 years, ≥ 75 years) including women with menstruation (aged 15-64 years) (aged ≥ 40 years) to eat lean meat and meats (beef, chicken, turkey), organ meats (beef liver, pork liver, sweetfish liver), seafood (oysters, sardines, tuna, lamprey eel, abalone, clams, snails, dried shrimp), potatoes (potato, konjac), nuts (cashew nuts, pistachio nuts, sesame seeds), grains (white rice, bread, spaghetti, brown rice, breakfast cereals fortified with 100% Daily Value iron), mushrooms (wood ear), legumes (kidney beans, white beans, lentils, green peas, chickpeas), seaweed (nori, hijiki), fruit (raisins, cantaloupes), vegetables (spinach, tomatoes, broccoli, parsley, ginger, chili pepper), dairy products (milk, cheese), soy products (tofu), eggs, dark chocolate, green tea, tea, cocoa to take in more iron to reach the RDAs established by the MHLW in Japan [41] or those established by the IOM of the National Academy of Sciences in the U.S. [42]. It must be careful not to exceed the ULs of the daily iron intake in Japanese men (aged ≥ 50 years) and women (aged ≥ 60 years).

Copper

The daily copper intake of Japanese people in 2022 was lower compared to that in 2001, 2004, 2007, 2010, 2013, 2016, and 2019 (2001: 1.25 mg/day; 2004: 1.19 mg/day; 2007: 1.16 mg/day; 2010: 1.12 mg/day; 2013: 1.12 mg/day; 2016: 1.11 mg/day; 2019: 1.12 mg/day; 2022: 1.09 mg/day). The daily copper intake was negatively correlated with the number of gout patients in 2001-2019 (r= -0.852, p= 0.0149) and in 2001-2022 (r= -0.875, p= 0.0044) (Table 1).

The daily copper intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 1.14 mg/day; 2022: 1.12 mg/day). The daily copper intake was negatively correlated with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= -0.818, p=0.0469) and in 2004-2022 (r= -0.863, p=0.0124) (Table 2). The daily copper 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: 1.23 mg/day; 2022: 1.20 mg/day, women: 2016: 2019: 1.07 mg/day; 2022: 1.05 mg/day). The daily copper intake was negatively correlated with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.890, p= 0.0176) and in 2004-2022 (r= -0.927, p= 0.0027) (Table 2). The daily copper intake was positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.880, p= 0.0207) (Table 2). Whereas the daily copper intake tended to be positively correlated with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2022 (r= 0.750, p= 0.0521) (Table 2). This result suggests that the correlation of daily copper intake with the number of gout patients varies with gender and is stronger in adult men than in adult women.

The daily copper intake of Japanese men (aged ≥ 15 years) and women (aged ≥ 15 years) in 2022 were 1.11-1.28 mg/day and 0.88-1.15 mg/day, respectively, and exceeded the RDAs established by the MHLW in Japan [men (aged ≥ 15 year): 0.8-0.9 mg/day; women (aged ≥ 15 year): 0.7 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 year): 0.89-0.90 mg/day; women (aged ≥ 14 year): 0.89-0.90 mg/day] [42]. The daily copper intake of Japanese men (aged ≥ 20 years) and women (aged ≥ 20 years) in 2022 were 1.11-1.26 mg/day and 0.88-1.15 mg/day, respectively, and were below the ULs established by the MHLW in Japan [men (aged ≥ 18 years): 7.0 mg/day; women (aged ≥ 18 years): 7.0 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 19 years): 10.0 mg/day; women (aged ≥ 19 years): 10.0 mg/day] [42]. The daily copper intake of Japanese men (aged 15-19 years) and women (aged15-19 years) were 1.28 mg/day and 0.96 mg/day, respectively, and were below the ULs established by the IOM of the National Academy of Sciences in the U.S. [men (aged 14-18 years): 8.0 mg/day; men (aged ≥ 19 years): 10.0 mg/day; women (aged 14-18 years): 8.0 mg/day; women (aged ≥ 19 years): 10.0 mg/day] [42]. In healthy men and women, taking of copper supplementation should be careful so as not to exceed the ULs.

Copper is metalloenzymes of superoxide dismutase (SOD) [22]. In a mendelian randomization study, blood copper concentration had no association with gout risk [88].

Copper-rich foods are meats (beef, turkey), organ meats (beef liver, turkey giblets), seafood (oysters, crab, salmon, dried shrimp, squid, dried squid, lamprey eel, octopus, river snails), whole grains (cereals, millet), grains (pasta), potatoes, legumes (chickpeas), seeds and nuts (cashew nuts, sesame seeds, chia seeds, sunflower seeds, Brazil nuts, perilla seeds, hazelnuts), mushrooms (maitake mushrooms, shiitake mushrooms), fruit (avocados, apples), vegetables (spinach, asparaguses, tomatoes), dairy products (low-fat yogurt, non-fat milk), soy products (tofu, yuba), baking chocolate, dark chocolate, cocoa, tea [47-49]. It seems that Japanese people (aged ≥ 15 years) need to decrease copper intake or pay attention to not to excessive intake of copper.

Zinc

The daily zinc intake of Japanese people in 2022 was lower compared to that in 2001 and 2019 and was higher compared to that in 2007, 2010, 2013, and 2016 and was the same as that in 2004 (2001: 8.5 mg/day; 2004: 8.3 mg/day; 2007: 8.2 mg/day; 2010: 7.9 mg/day; 2013: 8.0 mg/day; 2016: 8.0 mg/day; 2019: 8.4 mg/day; 2022: 8.3 mg/day). The daily zinc intake did not show a significant correlation with the number of gout patients in 2001-2019 (r= -0.304, p= 0.508) and in 2001-2022 (r= -0.138, p= 0.744) (Table 1).

The daily zinc intake of Japanese adult population (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 8.4 mg/day; 2022: 8.3 mg/day). The daily zinc intake did not show a significant correlation with the number of gout patients in the adult population (aged ≥ 20 years) in 2004-2019 (r= 0.162, p= 0.759) and in 2004-2022 (r= 0.325, p= 0.477) (Table 2). The daily zinc intake of Japanese adult men (aged ≥ 20 years) in 2022 was lower compared to that in 2019 (2019: 9.2 mg/day; 2022: 9.1 mg/day). The daily zinc intake did not show a significant correlation with the number of gout patients in adult men (aged ≥ 20 years) in 2004-2019 (r= -0.0973, p= 0.854) and in 2004-2022 (r= 0.050, p= 0.916) (Table 2). Whereas the daily zinc intake of Japanese adult women (aged ≥ 20 years) in 2022 was the same as that in 2019 (2019: 7.7 mg/day; 2022: 7.7 mg/day). The daily zinc intake did not show a significant correlation with the number of gout patients in adult women (aged ≥ 20 years) in 2004-2019 (r= 0.408, p= 0.421) and in 2004-2022 (r= 0.425, p= 0.341) (Table 2).

The daily zinc intake of Japanese men (aged ≥ 20 years) and women (aged 20-69 years, aged ≥ 80 years) in 2022 were 8.6-9.3 mg/day, 7.3-7.8 mg/day, and 7.3 mg/day, respectively and were below the RDAs established by the MHLW in Japan [men (aged ≥ 20 years): 10.0-11.0 mg/day; women (aged ≥ 20 years): 8.0 mg/day] [41] and those established by the IOM of the National Academy of Sciences in the U.S. [men (aged ≥ 14 years): 11.0 mg/day; women (aged 14-18 years): 9.0 mg/day; women (aged ≥ 19 years): 8.0 mg/day] [42]. The daily zinc intake of Japanese women (aged 70-79 years) in 2022 was 8.0 mg/day and reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

In a mendelian randomization study, blood zinc concentration had no association with gout risk [88].

In a cross-sectional study in middle-aged and older men (aged ≥ 40 years) and women (aged ≥ 40 years) in China, in the minimally adjusted model (adjusted for age, body mass index (BMI) and energy intake), increased zinc intake was associated with decreased hyperuricemia risk in middle-aged and older men, but not in women [SUA concentration ≥ 7.0 mg/dL (416.4 µmol/L) in men and ≥ 6.0 mg/dL (356.9 µmol/L) in women] [94]. However, in the multivariable adjusted model, there was no significant association between dietary zinc intake and hyperuricemia risk in both middle-aged and older men and women [94]. In the NHANES 2001-2014, the daily zinc intake was inversely associated with hyperuricemia risk among U.S. adult men (aged ≥ 20 years) and women (aged ≥ 20 years) [hyperuricemia: SUA concentration ≥ 7.0 mg/dL (416.4 µmol/L) in men and ≥ 6.0 mg/dL (356.9 µmol/L) in women] [21]. This article revealed that increased zinc intake was associated with decreased hyperuricemia risk among U.S. adult men (aged ≥ 20 years) but not in women (aged ≥ 20 years) [21]. There was no significant association between zinc intake and hyperuricemia risk in both men and women with hypertension or diabetes [21].

Zinc is metalloenzymes of superoxide dismutase (SOD) [22]. Zinc has the antioxidant activity [95]. Zinc in human plays an important role in cell mediated immunity and is also an antioxidant and anti-inflammatory agent [96]. Nicotinamide adenine dinucleotide phosphate (NADPH) oxidases in inhibited by zinc, leading to reduced generation of reactive oxygen species (ROS), zinc is able to bind to sulfhydryl groups of various molecules, protecting them from oxidation [96]. In *in vitro* study, UA stimulated an increase in nicotinamide adenine dinucleotide phosphate (NADPH) oxidase-derived reactive oxygen species (ROS) production in adipocytes, vascular smooth muscle cells, as well as vascular endothelial cells [97]. Zhang et al. [21] have stated that dietary zinc intake maybe negatively associated with hyperuricemia through the antioxidant activity.

Judging from the data of food composition [47-49], it is important for Japanese men (aged ≥ 20 years) and women (aged 20-69 years, aged ≥ 80 years) to eat meats (beef, pork), processed meats (beef jerky), organ meats (turkey breast, pork liver), seafood (oysters, blue crab, shrimp, salmon, dried bonito, king crab, carp, mackerel, anchovy, sardines, snails, scallop, lamprey eel), seeds and nuts (pumpkin seeds, peanuts, sesame seeds, flaxseeds, chia seeds), grains (breakfast cereals fortified with 25% Daily Value zinc, oatmeal, brown rice, bread), mushrooms (maitake mushrooms), legumes (lentils, kidney beans), seaweed, fruit (blueberries), vegetables (broccoli, cherry tomatoes), dairy products (milk, cheese, Greek yogurt), eggs, green tea and matcha, cocoa to take in more zinc to reach the RDAs established by the MHLW in Japan [41] and those established by the IOM of the National Academy of Sciences in the U.S. [42].

3.2. Effect of Dietary Antioxidant on SUA Concentrations, Hyperuricemia, or Gout

Composite dietary antioxidant index

Lin et al. [98] constructed a composite dietary antioxidant index (CDAI) consisting of food parameters for vitamin A, vitamin C, vitamin E, manganese, selenium, and zinc to represent an individual's antioxidant intake status. In a cross-sectional study including 8761 participants was conducted based on the NHANES 2007-2018, there was a significant negative association between composite dietary antioxidant index and hyperuricemia [SUA concentration ≥ 7.0 mg/ dL (416.4 μmol/L) in males and ≥ 6.0 mg/dL (356.9 μmol/L) in females] in the U.S. adults [98]. This article revealed that individuals in the second quartile (-1.177 to 0.796), third quartile (0.799 to 3.202), and fourth quartile (highest) (3.203 to 88.502) of composite dietary antioxidant index (CDAI) were 19%, 25%, and 35% decreased risk of hyperuricemia, respectively, compared to those individuals in the first quartile (lowest) of composite dietary antioxidant index (CDAI) (-7.177 to -1.178) [98].

Oxidative balance score

In twenty-one original articles shown in a review by Hern ández-Ruiz et al. [99], all oxidative balance scores included a higher number of antioxidant components than pro-oxidant components, suggesting that higher oxidative balance scores indicated beneficial oxidative balance and predominance of antioxidant components. Wang et al. [100] examined the associations of oxidative balance score (OBS) with hyperuricemia and gout in U.S. adults (aged ≥ 20 years) using data from the NHANES from 2007 to 2018. This study showed that oxidative balance score consisted of dietary (16 dietary nutrients: dietary fiber, carotene, riboflavin, niacin, vitamin B_6, total folate, vitamin B_{12}, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, total fat, iron) and lifestyle (BMI, physical activity, alcohol consumption, smoking status) components and oxidative balance score is in favor of antioxidants and lower oxidative balance score indicates higher exposure to oxidants. Higher OBS (dietary OBS + lifestyle OBS), dietary OBS, and lifestyle OBS were associated with lower risk of hyperuricemia [SUA concentration > 7.0 mg/ dL (416.4 μmol/L) in males and > 5.7 mg/dL (339.1 μmol/L) in females], respectively [100]. There was no significant association between OBS (dietary OBS + lifestyle OBS) or dietary OBS and gout risk [100]. Higher lifestyle OBS was associated with lower gout risk [100].

He et al. [62] also examined the association of OBS (dietary OBS + lifestyle OBS) with hyperuricemia and gout in U.S. adults (aged ≥ 20 years) using data from the NHANES 2009-2018. In this study, the OBS incorporated 16 nutrients and 4 lifestyle factors as follows: pro-oxidants are total fat, iron, alcohol consumption, BMI, and cotinine; antioxidants are dietary fiber, β-carotene, riboflavin, niacin, vitamin B_6, total folate, vitamin B_{12}, vitamin C, vitamin E, calcium, magnesium, zinc, copper, selenium, and physical activity [62]. There was a negative correlation between OBS (dietary OBS + lifestyle OBS) and plasma UA, hyperuricemia risk or gout risk, respectively [62]. Higher OBS (dietary OBS + lifestyle OBS), dietary OBS, and lifestyle OBS were associated with lower risk of hyperuricemia [SUA concentration ≥ 7.0 mg/ dL (416.4 μmol/L) in males and ≥ 6.0 mg/dL (356.9 μmol/L) in females], respectively [62]. Higher OBS (dietary OBS + lifestyle OBS) and lifestyle OBS were associated with lower gout risk, respectively [62]. However, there was no significant association between dietary OBS and gout risk [62]. Wang et al. [100] and He et al. [62] found that lifestyle OBS was more effective in reducing the risk of hyperuricemia compared to dietary OBS.

Wu et al. [101] have stated that the pathogenesis of hyperuricemia and gout is multifactorial and complex, involving a mix of genetic, environmental factors (e.g., microclimate, season, ambient/indoor air pollution and extreme weather), and dietary factors. Several environmental factors have shown the ability to induce the production UA and regulate the innate immune pathway, involving in the pathogenesis of gout [101]. The guidelines have stated that important lifestyle changes in gout patients include weight control [5, 81, 102-104], physical activity [5, 102, 103], smoking cessation [5], and proper hydration [5, 81, 103]. Therefore, it seems that practicing selection and intakes of foods rich in antioxidant nutrients, achievement and maintenance of ideal body mass index (BMI), weight loss for overweight and obese people, adequate physical exercise (e.g., moderate intensity aerobic exercise for 30 minutes on 5-7 days per week, vigorous intensity aerobic physical activity for 75 minutes per week), smoking cessation, and proper hydration are essential for the prevention of gout. Cardiovascular disease (CVD) is hyperuricemia-related diseases [2], comorbidities of hyperuricemia and gout [1], and diseases implicated in oxidative stress [2, 16]. The contents of above-mentioned lifestyle (weight management, moderate intensity aerobic exercise, and smoking cessation) are consistent with those of healthy adults for the prevention of CVD recommended by the World Health Organization [105]. Since maintaining SUA concentrations 2.0-4.0 mg/dL (119.0-237.9 μmol/L), which have antioxidant activity, may help prevent not only hyperuricemia and gout, but also CVD, it seems that modifications of dietary nutrient (especially antioxidant) intakes and lifestyle are important for the prevention of the above-mentioned diseases in individuals with or without hyperuricemia.

4. Conclusions

The number of gout patients of Japanese people in 2022 was higher compared to that in 2019 and increased 5.12-fold compared to that in 1986 (1986: 0.255 million; 2019: 1.254 million; 2022: 1.306 million) [33-35]. The daily intake of vitamin E, vitamin K, and pantothenic acid of Japanese people in 2022 were higher compared to those in 2019, respectively. Whereas the daily intake of vitamin A, vitamin D, vitamin B_2, niacin, vitamin B_6, folate, vitamin B_{12}, vitamin C, sodium, salt, calcium, potassium, magnesium, phosphorus, iron, copper, and zinc of Japanese people in 2022 were lower compared to those in 2019. The daily intake of vitamin B_1 of Japanese people in 2022 was the same as that in 2019. The daily intake of vitamin A, vitamin D, vitamin E, vitamin B_1, vitamin B_2, folate, vitamin B_{12}, vitamin C, salt, calcium, iron, and copper were negatively correlated with the number of gout patients, respectively (Table 1). The daily niacin intake was positively correlated with the number of gout patients (Table 1).

Based on the results of relationship between the number of gout patients and micronutrient (vitamin and mineral) intake and evaluation of the daily dietary nutrient intake of Japanese people using Dietary Reference Intakes definitions set by the MHLW in Japan [41] and the IOM of the National Academy of Sciences in the U.S. [42, 43], modification of micronutrient intake for the prevention of gout in Japanese people (especially adults) in 2022 is suggested as follows: limiting or decreasing intake of sodium and salt; decreasing intake of niacin; decreasing or pay attention to not to excessive intake of vitamin K, pantothenic acid, vitamin B_{12}, phosphorus, and copper; increase intake of vitamin A, vitamin D, vitamin E, vitamin B_1, vitamin B_6, folate, calcium, potassium, and magnesium; increase intake of vitamin B_2 in Japanese men (aged 15-59 years) and women (aged 15-49 years), vitamin C in Japanese men (aged 20-59 years) and women (aged 20-49 years), iron in Japanese men (aged 20-59 years) and women (aged 20-69 years, $\geq$ 75 years), and zinc in Japanese men (aged $\geq$ 20 years) and women (aged 20-69 years, aged $\geq$ 80 years). It seems that modification of lifestyle (weight management, moderate intensity aerobic exercise, and smoking cessation) play an important role in the prevention of gout including the above-mentioned dietary modification.

Further research is necessary to assess to what extent SUA concentrations change by the differences in dietary patterns under the condition of daily nutrient intake reach the RDAs or the AIs established by the IOM of the National Academy of Sciences in the U.S. in individuals without and with hyperuricemia or gout in randomized controlled trials.

Abbreviations

AI	Adequate Intake
CVD	Cardiovascular Disease
EAR	Estimated Average Requirement
IOM	Institute of Medicine
MHLW	Ministry of Health, Labour and Welfare
NHANES	National Health and Nutrition Examination Survey
OBS	Oxidative Balance Score
RDA	Recommended Dietary Allowance
SUA	Serum Uric Acid
UL	Tolerable Upper Intake Level
SUA	Uric acid

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Data Availability Statement

The data that support the findings of this study are as follows:

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Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

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Research Field

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