3.6. Concomitant Use of Dietary Supplements and Medicines

Most ambulatory patients (91.3%) and admitted patients (81.8%) took medicines; in contrast, only 10.6% of healthy subject took medicines (Table 4). Furthermore, 36.8% of ambulatory patients, 17.7% of admitted patients, and 4.3% of healthy subjects took dietary supplements and medicines concomitantly.

Table 4. Concomitant use of dietary supplements and medicines.

	Medicines *n* **(%)**	**Dietary Supplements** *n* **(%)**	**Parallel Use** *n* **(%)**
Healthy Subjects ($n = 979$)	104 (10.6)	301 (30.7)	42 (4.3)
Ambulatory Patients ($n = 1154$)	1054 (91.3)	451 (39.1)	425 (36.8)
Admitted Patients ($n = 599$)	490 (81.8)	122 (20.4)	106 (17.7)

Table 5 shows the number of subjects taking concomitant dietary supplements and medicines. The most common pattern was one kind of dietary supplement and one kind of medicine ($n = 44$). However, six subjects took more than five dietary supplements and more than five medicines concomitantly.

Table 5. Number of dietary supplements and medicines used concomitantly.

Number of	**Number of Medicines**				
Dietary Supplements	1	2	3	4	5≤
1	44	43	27	28	37
2	43	40	33	14	32
3	16	17	13	8	13
4	4	4	3	2	4
5≤	10	5	3	3	6

$n = 452$; Missing values were excluded.

3.7. Declaration of Dietary Supplements Use to Primary Care Doctors

In patients who took dietary supplements and medicines concomitantly, only 30.2% of admitted patients and 28.0% of ambulatory patients declared their use of dietary supplements to their attending physicians. In other words, almost 70% of patients used dietary supplements on their own, without consulting physicians. Table 6 shows reasons for no declaring dietary supplements use to physicians in each ambulatory and admitted patient.

Table 6. Reasons for not discussing dietary supplement use with physicians.

Reasons	**Ambulatory (*n*)**	**Admitted (*n*)**
Dietary supplements that they use does not relate to their treatment	25	2
Doctors might deny dietary supplements use	19	2
Doctors never ask about dietary supplements use	14	5
Dietary supplements are just food	16	2
No need to say	7	6
There are any influences to medication (self-judgment)	8	1

Table 6. *Cont.*

There are not any opportunities to tell	5	1
Doctors do not have any knowledge about dietary supplements	3	1
There are not any problems in using dietary supplements	3	0
Use dietary supplements only as needed	3	0
Other	12	4

$n = 112$ in ambulatory patients and $n = 24$ in admitted patients; Subjects answered this question.

4. Discussion

In this study, we clarified that not only ambulatory patients but also admitted patients used dietary supplements, and they used it for treatment their diseases. These patients also took medicines concurrently without consulting physicians.

In the United States, 48.8% of people used dietary supplements from 2007 to 2010 [10]. Previous reports show that use of dietary supplements in Japan has increased over time from 10.9% in 2001 [11], 11.0% in males and 16.4% in females in 2003 [12], and 45.8% in older adults in 2008 [9], even if factors such as sex, age, socioeconomic status, and health-related characteristics are known to affect use of dietary supplements [10,13–16]. In addition, recognition also affects dietary supplement use. Dietary supplements were not regulated in Japan. Most dietary supplements are the form of capsules, tablets, powders, or liquid, and some are the form of regular foods in Japan. In this situation, some people take dietary supplements without consideration for the risk of them. In these days, as dietary supplement use increases, associated health problems also increase. Health problems associated with dietary supplement use have two causes. One is use of low quality or illegal products that contain drug ingredients [17,18]. To avoid health problems caused by these products, the Japanese government constantly surveys and checks these products on websites and retail stores. Another is inappropriate use of dietary supplements, including excessive intake and concomitant use of various dietary supplements and/or medicines. In particular, inappropriate use of dietary supplements in patients may be associated with severe health problems. To avoid health problems caused by inappropriate use, communication between patients and physicians are important.

It is recognized that infants, children, pregnant women, the elderly, and patients are susceptible to dietary supplements. It is important to identify dietary supplement use in these high-risk groups and to stop inappropriate use. Inappropriate use of dietary supplements by Japanese children [19] and pregnant women [20] has been defined. In Japan, most children have a good nutritional state and thus do not require dietary supplements. On the other hand, folic acid supplements are recommended for pregnant women because it is difficult to obtain adequate amounts of folic acid from food [21]. However, we confirmed that pregnant women could not avail of dietary supplements appropriately [20]. Aside from children and pregnant women, many older people in Japan appear to use dietary supplements; some of them use dietary supplements for treatment of diseases [22]. In this study, we investigated the awareness and use of dietary supplements among Japanese subjects.

Our results showed that 36.8% of ambulatory patients and 17.7% of admitted patients took dietary supplements with their medicines and thought that this practice was safe. However, many reports indicate that dietary supplements interact with medicines. The most well-known example is St. John's

wort (*Hypericum perforatum* L.). St. John's wort contains hyperforin, which increases the expression of cytochrome P450 (CYP), especially CYP3A4, and affects drug metabolism in the liver [23]. Other herbs (e.g., black cohosh, coleus forskohlii, echinacea, garlic, ginkgo, ginseng, green tea, kava, and milk thistle) [24–28] and ingredients (e.g., catechins [29], curcuminoids [30], isoflavones [31], quercetin [32], polyphenols [33], and resveratrol [34]) also affect drug metabolizing enzymes.

To avoid interactions between prescription medications and dietary supplements, physicians need to know whether their patients use dietary supplements or not. However, as shown in this survey, most patients do not discuss these supplements with their physicians, which is consistent with previous reports [35]. One reason for this lack of discussion is that most physicians do not ask about dietary supplement use, probably because the consultation time for each patient is limited. In addition, 5 admitted patients answered "Doctors never ask about dietary supplements use" (Table 6), it means that some of physicians did not care whether their patients used dietary supplements or not. It might be caused by insufficient recognition of dietary supplements. At the same time, most patients do not think that dietary supplements will affect their medication. Thus, both patients and physicians do not fully recognize the risk of interactions between dietary supplements and medications [36]. It is also reported that both of patients and physicians are poorly understood the regulation of dietary supplement in the USA [37], even though dietary supplements are regulated by the U.S. Food and Drug Administration (FDA) under Dietary Supplement Health and Education Act. As dietary supplements are not as safe as they believe [38], education for both physicians and patients is important in order to avoid health problems associated with dietary supplements.

Consistent with a previous internet survey in Japan, 3.3% of all subjects experienced adverse effects by using dietary supplements, even if most cases were not severe. In this survey, we did not ask which type of product was used. Thus we could not determine any relationship between dietary supplements and adverse effects. However, many subjects used several dietary supplements and medicines concurrently. Even if we asked which type of product was used, it would be impossible to determine the cause of health problems. To avoid unexpected health problems caused by dietary supplements, patients should not use dietary supplements for disease treatment or concurrently with medicines without consulting by physicians.

There are some limitations in this study. The number of admitted patients was lower than the number of ambulatory patients or healthy subjects, because cooperation with primary doctors was essential to conduct this survey in admitted patients. In addition, we did not ask type, periods, and frequency of dietary supplements use or medications. So, we could not evaluate the exact risk of concomitant use of dietary supplements and medicines in this study. Further investigations are needed.

5. Conclusions

We clarified that most patients used dietary supplements without consulting physicians, and some of them experienced adverse effects from using dietary supplements. To avoid health problems, it is important that physicians ask patients about dietary supplement use and those patients should inform their physicians about these supplements if physicians do not ask.

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Author Contributions

Tsuyoshi Chiba formulating the research question, designing the study, carrying it out, analyzing the data, and writing the article; Yoko Sato carrying it out and analyzing the data; Tomoko Nakanishi, Kaori Yokotani, and Sachina Suzuki carrying it out; Keizo Umegaki designing the study and writing the article.

Conflicts of Interest

The authors declare no conflict of interest.

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