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ORIGINAL ARTICLE

Patients' perspectives on generic substitution among statin users in Japan

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Abstract

Aim The study was undertaken to reveal the differences in statin users' characteristics, the views on generic drugs between brand-name statin users and generic statin users, and the factors associated with being generic statin users.

Subjects and methods A questionnaire survey was conducted on patients visiting community pharmacies in order to have their prescriptions including statins dispensed. Respondents answered their views on the questionnaire items using a 5-point Likert-type scale, then answers were dichotomized. Odds ratios were calculated to analyze respondent's views and respondents' characteristics associated with being generic users.

Results In total, 122 patients agreed to participate in the survey; with regard to respondent's views associated with being generic statin users, those agreeing "I have a concern in switching any currently taken drugs to generic drugs" were less likely to be generic statin users [OR (95% CI): 0.13, (0.05–0.35)]. Respondents agreeing "generic drugs are less expensive than brand-name drugs" were more likely to be generic users [4.55, (1.77–11.67)]. No respondent's characteristics were associated with being generic statin users. The majority of respondents agreed "I don't mind taking the generic drugs that my physician prescribe". With regard to how much cost savings would encourage them to substitute, 1000–1999 Japanese Yen per pharmacy visit was most often indicated by the respondents.

Conclusion A certain level of cost saving is necessary for patients to substitute. Physician-initiated substitution reduce patients' concerns in switching. The introduction of a kind of policy to widen the price difference between brand-name drugs and generic drugs should be considered as one of the policy options.

Keywords Generic substitution · Pharmaceutical policy · Patient medication knowledge · Questionnaire survey

Introduction

Control of escalating medical expenditure is a common urgent issue throughout the world (Alrasheedy et al. 2014; Dunne and Dunne 2015). Encouraging generic drug substitution as one of the foremost measures for controlling prescription drug costs is supported by health authorities in various countries. Japan is no exception. The total national medical care expenditure in Japan increased to 40.8 trillion Japanese yen (hereinafter termed JPY) in 2014 from 32.1 trillion JPY in 2004 (MHLW 2014a). Various policies and measures by the Japanese government have promoted the use of generic drugs, the share of which has increased to 56.2% in 2015 (volume share) from 32.5% in 2005 (MHLW 2017a). However, the volume share of generic drugs in Japan is still low compared to other developed countries; it is 84% in the United States, 83% in the United Kingdom (OECD 2015). The Japanese government announced the revised "Roadmap for further promotion of the use of generic drugs" in 2013 which set a new target for the generic share (volume share) to be 60% by March 2018 (MHLW 2013). Further, the Cabinet of Japan has strongly promoted the policy, and has suggested an accelerated challenging target of 80% of the generic share (volume share) by September 2020 (MHLW 2017b).

To widen the use of generic drugs, the acceptance of generic drugs by patients is an essential issue, since patients are the end users of generic drugs (Dylst et al. 2013). Many studies in the literature have shown that patients or general public prefer brand-name drugs over generic drugs (Kobayashi et al. 2011; Hoshi and Kimura 2008; Shrank et al. 2009; Keenum

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et al. 2012; Lebanova et al. 2012; Sewell et al. 2012; Ibrahim et al. 2012). In a study on the general public in the United States, Shrank et al. (2009) reported that 94% of the respondents believed that generic drugs were less expensive than brand-name drugs, and more than 70% of them agreed that "generic drugs are better value than brand-name drugs". However, they found out that only 37.6% of the respondents agreed that "they would rather take generic than brand-name medications". Also in a study in Australia, 81% of the respondents agreed that generic drugs were less expensive than brand-name drugs, but those agreeing to preferably take generic drugs over brand-name drugs accounted for only 29.7% (Ibrahim et al. 2012). In Japan, 68.4% of Japanese public knew "generic drugs", 86.0% of them agreed that "generic drugs are less expensive than brand-name drugs" and 54% of them showed their willingness for generic substitution. Interestingly, only 18.4% of them had used generic drugs (Kobayashi et al. 2011). Even if the patient has a correct understanding and recognizes the cost benefit of generic drugs, it does not necessarily lead to them actually substituting generic drugs in place of brand-name drugs. This concept has been summarized in a title as "generic medications for you, but brand-name medications for me" (Keenum et al. 2012).

Although, it is evident that the price difference between brand-name drugs and generic drugs is a major factor influencing patients' choice (Alrasheedy et al. 2014), if the price difference between brand-name drugs and generic drugs is small, patients prefer to use the original drugs (Alrasheedy et al. 2014). Thus, a copayment system reflecting the differential cost between brand-name drugs and generic drugs plays an essential role from the viewpoint of the patient. The reference pricing system, which has been introduced in several European countries (Giuliani et al. 1998; Brekke et al. 2009; Drozdowska and Hermanowski 2016; Rathe et al. 2013) has not been introduced in Japan. The price of generic drugs is initially set by the Ministry of Health, Labour and Welfare Japan as 50% of the brand-name drug price at the time of the first generic approval after the expiration of the brand-name drug's patent period (or 40% if the number of competitor generic drugs is over 20) (MIHW 2016). Although a community pharmacist is committed to substituting prescribed drugs with generic drugs, the patient or prescribing doctor has the freedom to refuse such a substitution. Even if a patient refuses generic substitution and obtains the brand-name drug, they only pay the drug price depending on a fixed copayment (as a general rule, 20% for preschool children & those aged 70 to 74, 10% for those at age of 75 & over, 30% for the others) regardless of whether they receive brand-name drugs or generic drugs. A patient preferring brand-name drugs does not need to pay the difference in price, unlike the reference pricing system which has been introduced in several European countries such as Denmark, Germany, Norway, Poland etc. (Giuliani et al. 1998; Brekke et al. 2009; Drozdowska and Hermanowski 2016; Rathe et al. 2013). Under such a situation in Japan, the price difference that the patient really pays from their out-of-pocket money is not as large as the true price difference between brand-name drugs and generic drugs.

Based on a survey of the National Federation of Health Insurance Societies (MHLW 2011), when people were informed of the difference in copayment if they were to substitute their prescription drugs, 12.0–14.5% of them decided to change their drugs to generic drugs. The share in use of generic drugs has increased to 21.5% (2011) from 13.1% (2009) according to one health insurer, and to 23.3% (2010) from 19.5% (2008) from another health insurer (MHLW 2011). Further, another health insurer stated that among insured patients with chronic conditions including hypertension, hyperlipidemia, and diabetes, 34.7% of them decided to change to generic drugs, and that 68% of the reduction of drug cost was attributed to generic substitution of drugs for chronic conditions (MHLW 2011). In another Japanese study based on a medical insurance claim database of community pharmacies, generic drugs tended to be selected as the price difference increased (Takizawa et al. 2015).

The above-mentioned group of patients with chronic diseases should be considered by health-care professionals. These patients must take drugs for a lengthy period, and thus the use of generic drugs will provide substantial cost savings (Alrasheedy et al. 2014). Although previous studies are available concerning patients or the general public based on their knowledge on generic drugs or their attitudes and preference of generic drugs, few studies on attitudes and preferences of chronic disease patients towards generic drugs in Japan have been reported. We focused on hyperlipidemia, since patients diagnosed with hyperlipidemia rely on cholesterol-lowering drugs, such as 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors (hereinafter "statins") to manage their chronic condition (Sarpong and Zuvekas 2014). Pravastatin, simvastatin, fluvastatin, atorvastatin, pitavastatin and rosuvastatin are available in the Japanese market as statins (in the year 2016). Of these, generic drugs are also available in the market for all statins, with the exception of rosubastatin. The price of the brand-name drugs is nearly twice the price of corresponding generic drugs; thus, cost saving over a long period would be substantial.

The aim of this study is to reveal the differences in characteristics and views between brand-name statin users and generic statin users and to explore the factors associated with being generic statin users.

Methods

Study settings

A cross-sectional questionnaire survey with a pharmacy clinical record survey was carried out on statin-user patients from

March 2015 to March 2016. Patients who brought their prescription (which included one of the subject statins) to one of two community pharmacies located in Chiba, Japan were recruited. The subject statins were pravastatin, simvastatin, atorvastatin, pitavastatin and fluvastatin, for which both brand-name drugs and generic drugs were in the market in Japan. The community pharmacies were the pharmacies collaborating with clinical research by the researchers of the School of Pharmaceutical Sciences of Chiba University. Patients for whom this was the first visit during the past 6 months were excluded from the study, since previous clinical records were not available. During their visit to the pharmacy, the researchers approached the patients, explained the study, stated that all responses would be anonymous and requested they complete the questionnaire in the pharmacy. Patients' consent to participate was indicated by returning the completed questionnaire. The study was approved by the research ethics committee of Graduate School of Pharmaceutical Sciences, Chiba University.

Data collection

The following data were extracted from the pharmacy clinical record: gender, age, copayment rate of pharmacy fee, drugs dispensed in the past 6 months from the day of the visit. A self-administered anonymous questionnaire with multiple choice (single answer unless otherwise specified) questions was developed on the basis of a literature review (Keenum et al. 2012; Lebanova et al. 2012; Ibrahim et al. 2012; Wong et al. 2014; O'Leary et al. 2015; Rathe et al. 2015); The questionnaire was composed of the following three sections: 1) respondent's views on generic drugs and respondent's experiences with generic substitution, 2) respondent's attitudes towards generic substitution and how significantly the cost reduction would encourage them to substitute, and 3) respondent's characteristics. The answers on respondent's views on various aspects of generic drugs were measured on the five-point Likert scale ("agree", "somewhat agree", "neutral", "somewhat disagree" and "disagree").

Statistical analysis

Descriptive statistics were used to describe: 1) respondent's views and experiences regarding generic drugs, 2) respondent's attitudes towards generic substitution and how significantly this cost reduction would encourage them to substitute, and 3) respondent's characteristics. All costs were in Japanese yen (JPY) and were converted into US dollars (USD) (2016) using Federal Reserve historical foreign exchange rates:1 US$ = ¥ 108.66 (Federal Reserve 2018). Although the respondents answered six statements regarding their views (generic drug's effectiveness, quality, side-effects, expensiveness, concerns, and contribution on national medical expenditure) using the 5-point Likert-type scale, the answers were dichotomized. Consistent with the coding scheme used by Shrank et al. (2009), respondents were considered to "agree" if they "agree" or "somewhat agree" to an item, and "others" if their response was "disagree", "somewhat disagree", or "neutral". Chi-square tests were used to evaluate and compare respondents' characteristics and views, experiences, and attitudes towards generic drugs between brand-name statin users (hereinafter "BR statin users") versus generic statin users (hereinafter "GE statin users").

To analyze factors associated with being GE statin users, odds ratios were calculated. To explore respondents' views of generic drugs associated with being GE statin users, respondents' views of six statements regarding generic drugs were dichotomized as mentioned above. To explore respondents' characteristics associated with being GE statin users, variables of gender (male, female), age (< 70, 70 and over), copayment rate (0–20%, 30%) and visiting another pharmacy (no, yes) were dichotomized. The odds ratios for being GE statin users versus BR statin users were calculated and 95% confidence intervals were derived. All of these statistical analyses were performed by SPSS ver. 20.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 122 patients (median age 70 years; 68% females) agreed to participate in the survey (Table 1). Atorvastatin and pravastatin were the most used statins among the respondents; 73.0% of them were GE statin users. Copayment rate was 10% for 43.4% of the respondents and 30% for 50.8% of them; 45.1% of them had visited another community pharmacy during the past 6 months.

Between BR statin users ($N = 33$) and GE statin users ($N = 89$), no differences were observed in distributions of gender, age, copayment rate, and visiting of another pharmacy. The median age was 70 years old for both BR statin users and GE statin users. BR statin users were more likely to have experience of switching back to brand-name drugs from generic drugs ($P < 0.05$). BR statin users were more likely to agree that generic drugs were less effective than brand-name drugs and that generic drugs were of inferior quality to BRs ($P < 0.01$). Further, almost half of BR statin users had concerns in switching from current drugs to generic drugs (48.5%), much more than GE statin users (11.2%, $P < 0.001$). With regard to cost of generic drugs, GE statin users were more likely to agree with the statement "generic drugs are less expensive than brand-name drugs" than were BR statin users ($P < 0.01$) (Table 2).

These findings were further confirmed by odds ratio analysis (Table 3). None of the patient characteristics (age, gender, copayment rate, and visiting another pharmacy) were associated with being GE statin users, whereas with regard to patients' views on generic drugs, the respondents agreeing "generic

Table 1 Characteristics of the respondents ($N = 122$)

Characteristic		*N*	%
Gender			
	Male	39	32
	Female	83	68
Age: median (range)	70 (42–90)		
Age groups			
	41–50	6	4.9
	51–60	14	11.5
	61–70	39	32
	71–80	54	44.3
	81–	9	7.4
Copayment rate			
	0%	1	0.8
	10%	53	43.4
	20%	6	4.9
	30%	62	50.8
Visited another pharmacy during the past 6 months			
	Yes	55	45.1
Are you/family members health care professionals?			
	Yes	26	21.3
	No	90	73.8
	Missing	6	4.9
Statins in use			
	Atorvastatin	45	36.9
	Pravastatin	37	30.3
	Pitavastatin	35	28.7
	Simvastatin	4	3.3
	Fluvastatin	1	0.8
Generic statins/brand-name statins in use			
Generic statins		89	73.0
brand-name statins		33	27.0

* health care professionals: someone such as a doctor, nurse, dentist, etc., whose job involves people's health

drugs are less expensive than brand-name drugs" were more likely to be GE statin users [OR (95% CI), 4.55 (1.77–11.67)]. This is the largest odds ratio of being GE statin users among patients' views on generic drugs. The respondents agreeing "Generic drugs are less effective than brand-name drugs" or "Generic drugs are of inferior quality to brand-name drugs" were less likely to be GE statin users [OR (95% CI), 0.09 (0.02–0.37), 0.17 (0.05–0.64), respectively]. The respondents agreeing "I have a concern in switching any current taking drugs to generic drugs" were also less likely to be GE statin users [OR (95% CI), 0.13 (0.05–0.35)]. Respondents' views on other aspects of generic drugs (more side-effects and reduction of national medical care expenditure) were not significantly associated with being GE statin users.

The average copayment of pharmacy fee per month during the last 6 months is shown in Table 4. Copayments of the majority of the respondents (69.7% of GE statin users, 81.8% of BR statin users) were lower than 3000 JPY (= 27.6 US$). No significant difference was observed in the percentage of respondents whose copayment was lower than 3000 JPY between BR statin users and GE statin users. Also no significant difference was observed in the mean (±S.D.) copayment, 2155.7 ± 1846.0 JPY (= 19.8 ± 17.0 US$) for BR statin users and 2470.6 ± 1984.8 JPY (= 22.7 ± 18.3 US$) for GE statin users.

With regard to the attitudes towards generic substitution between BR statin users and GE statin users (Table 2), GE statin users were more likely to agree to be willing to use generic drugs as often as possible compared to brand-name users ($P < 0.001$). Excluding the above-mentioned respondents (those agreeing to use generic drugs as often as possible) and those who did not answer the question concerning the attitudes towards generic substitution, the rest of the respondents were then asked how much cost saving per pharmacy visit would encourage them to substitute ($N = 54$, Table 5). A cost saving of 1000–1999 JPY (= 9.2–18.4 US$) per pharmacy visit was indicated first by the respondents (18.5%) and 500–999 JPY (= 4.6–9.2 US$) was indicated next (14.8%). A certain level of cost saving may be necessary to encourage them to substitute. However, 16.7% of the respondents indicated that they would never substitute, regardless of the cost saving. Fifty-four respondents (all the patients excluding those agreeing to use generic drugs as often as possible, as mentioned above) were also asked what factor would encourage them to substitute (multiple answers were allowed); 70.4% agreed that they did not mind taking the generic drugs prescribed by their physician. Further, some indicated the following: "I don't mind taking the generic drugs that a brand-name drugs company manufactures" (31.5%) and "I don't mind taking generic drugs which have been improved for easy administration" (22.2%) (data not shown).

Discussion

Statins are some of the most commonly prescribed drugs worldwide (Ramkumar et al. 2016) and the substitution from brand-name statins to generic statins could yield a large saving in drug costs (Salami et al. 2017; Slazak et al. 2016). This study assessed the factors associated with being GE statin users among Japanese BR/GE statin users.

No statistical differences were observed in patient characteristics (gender, age, copayment rate) between BR statin users and GE statin users. In previous studies on generic substitution in users of antidepressants and antiepileptics, 20- to 29-year-old drug users were more likely to agree to a generic switch compared to the 40- to 49-year-old users (Rathe et al. 2015). Also in an Australian study, younger patients (55 years or less) asked for generic drugs more often than older patients (Ibrahim et al. 2012). However, among the respondents of statin users in

Table 2 Characteristics, views, and attitudes towards generic drugs between generic statin users and brand-name statin users

		GE statin users		BR statin users		*P*
		N	%	*N*	%	
Total		89	100	33	100	
Respondent's characteristics						
Gender	Male	30	33.7	9	27.3	0.33[b]
	Female	59	67.3	24	72.7	
Age	Under 70	44	49.4	15	45.5	0.43[b]
	70 and over	45	50.6	18	54.5	
Copayment rate						
	0	1	1.1	0	0	
	10%	37	41.6	16	48.5	
	20%	4	4.5	2	6.1	
	30%	47	52.8	15	45.5	0.54[c]
Visited another pharmacy during the past 6 months						
		44	49.4	11	33.3	0.09[b]
Views and experiences of generic drugs						
Views of generic drugs[a]						
Generic drugs are less effective than brand-name drugs.		3	3.4	9	27.3	$P < 0.01$[b*]
Generic drugs are of inferior quality to brand-name drugs.		4	4.5	7	21.2	$P < 0.01$[b*]
Generic drugs produce more side-effects than brand-name drugs.		4	4.6	4	12.1	0.21[b]
Generic drugs are less expensive than brand-name drugs.		77	87.5	20	60.6	$P < 0.01$[b*]
I have a concern in switching any currently taken drugs to generic drugs.		10	11.2	16	48.5	$P < 0.01$[b*]
Generic substitution will contribute to reducing national medical expenditure.		65	73.9	28	87.5	0.14[b]
Experience of switching back to brand-name drugs from generic drugs						
		6	6.7	8	24.2	0.02[b*]
Attitudes towards generic substitution						
I am willing to use generic drugs as often as possible.		58	65.2	7	21.2	$P < 0.01$[d*]
I don't mind using generic drugs depending on explanation by medical staffs.		21	23.6	11	33.3	
I am not very willing to use generic drugs.		7	7.9	4	12.1	
I will not use generic drugs.		1	1.1	3	9.1	
I have not thought about this matter yet		1	1.1	3	9.1	
No answer		1	1.1	2	6.1	

[a]: # and % of the respondents agreeing or somewhat agreeing with the given statement

[b]: Chi-square test

[c]: Chi-square test, 30% vs others

[d]: Chi-square test, those choosing "I am willing to use generic drugs as much as possible" vs those choosing others or none

*: $P < 0.05$

the present study, 93% of them were over 50, none of them were in the 20- to 39-year-old group, and their median was 70 years old. The age distribution of the respondents was consistent with the age distribution previously reported in 2 million hyperlipidemia patients in Japan — 93.4% over the age of 50, and 44.8% over the age of 70 (MHLW 2014b). Thus, based on the majority of hyperlipidemia patients being over age 50, no difference was observed in the age distribution between BR statin users and GE statin users. This is also in line with a previous study (Mano et al. 2015) that found no difference in the age distribution of BR/GE atorvastatin users.

In this study, patients agreeing that "generic drugs are less effective than brand-name drugs" or "generic drugs are of inferior quality to brand-name drugs" were more likely to use BR statins. Previous studies on the association between patients' views and their willingness of substitution showed that misconceptions and negative perceptions on generic drugs among patients were reported to be the major obstacles to the acceptance of generic substitutions (Alrasheedy et al. 2014; Sewell et al. 2012; O'Leary et al. 2015; Al-Gedadi et al. 2008; Heikkilä et al. 2007). The finding in the present study that patients who reported negative views on generic drugs

Table 3 Odds ratio analysis of predictors of GE statin users: respondents' views of generic drugs and respondents' characteristics.

		OR	95% CI	*P* value
Generic drugs are less effective than brand-name drugs.	[a]	0.09	0.02–0.37	$P < 0.01^*$
Generic drugs are of inferior quality to brand-name drugs.	[a]	0.17	0.05–0.64	$P < 0.01^*$
Generic drugs produce more side effects than brand-name drugs.	[a]	0.35	0.08–1.49	0.15
Generic drugs are less expensive than brand-name drugs.	[a]	4.55	1.77–11.67	$P < 0.01^*$
I have a concern in switching any currently taken drugs to generic drugs.	[a]	0.13	0.05–0.35	$P < 0.01^*$
Generic substitution will contribute to reducing national medical care expenditure.	[a]	0.40	0.13–1.28	0.12
Age 70 and over	[b]	0.85	0.38–1.90	0.70
Female	[b]	0.74	0.30–1.78	0.50
Visit another pharmacy	[b]	1.95	0.84–4.53	0.12
Copayment, 30%	[b]	1.34	0.60–2.99	0.47

OR, odds ratio reflecting the likelihood of being GE statin users versus BR statin use:

CI, confidence interval, * $P < 0.05$

[a] Respondents' views of the given statements (those agreeing or somewhat agreeing with each statement)

[b] Respondents' characteristics (age, gender, visit another pharmacy, copayment rate 30%)

were more likely to be BR statin users is in line with the findings of the previous studies.

The respondents having concerns in switching their current drugs to generic drugs were more likely to be BR statin users, not GE statin users. With regard to the factors encouraging these respondents to substitute, one factor was that they did not mind using the generic drug if their physician had prescribed it. This is consistent with previous findings that patients would accept physician-initiated substitution (Kobayashi et al. 2011; Drozdowska and Hermanowski 2016; Al-Gedadi et al. 2008; Quintal and Mendes 2012; Al Ameri et al. 2011). Another benefit of physician-initiated substitution is the enhanced communication between physicians and patients on generic drugs in general. Patients will be able to clear concerns on generic drugs and build confidence in the use of generic drugs through communication with their physician. Such a physician-initiative situation is essential to prevent confusion and concerns of the patient during the process of generic substitution and to encourage patients to substitute; without such communication, patients are often faced with a situation where the physician prescribes "some medicine" and the pharmacist offers "another medicine" (Alrasheedy et al. 2014). That causes the patient to be confused and have concerns about the switch. Currently in Japan, physicians are not required to prescribe generic drugs, and they receive only 20 JPY (= 0.2 US$) when writing prescriptions by a generic name. A type of policy framework which encouraged physicians to write prescriptions for the generic version of a drug could be powerful in leading to patients switching without concern.

Table 4 Average copayment of pharmacy fee (per month, last 6 months)

(JPY)	Generic users		Brand-name users	
	N	%	*N*	%
< 1000	22	24.7	8	24.2
1000 to < 2000	25	28.1	13	39.4
2000 to < 3000	15	16.9	6	18.2
3000 to < 4000	11	12.4	2	6.1
4000 to < 5000	7	7.9	2	6.1
5000 to < 6000	3	3.4	0	0.0
6000 to < 7000	2	2.2	0	0.0
7000 to < 8000	3	3.4	1	3.0
8000 to < 9000	0	0.0	1	3.0
9000 to < 10,000	0	0.0	0	0.0
10,000 or higher	1	1.1	0	0.0
Mean ± SD	2470.6 ± 1984.8		2155.7 ± 1846.0	

Table 5 "How much cost saving per pharmacy visit would encourage you to substitute?" ($n = 54$)

	N	%
1–9 (JPY)	3	5.6
10–99 (JPY)	1	1.9
100–299 (JPY)	2	3.7
300–499 (JPY)	2	3.7
500–999 (JPY)	8	14.8
1000–1999 (JPY)	10	18.5
2000–2999 (JPY)	3	5.6
3000 and higher (JPY)	2	3.7
I would never substitute regardless of cost saving	9	16.7
No answer	14	25.9

This question was asked to all the respondents excluding those agreeing "I am willing to use generic drugs as often as possible" and those who didn't answer in the question of attitudes towards generic substitution

Two interesting aspects of respondents' views were found in the odds ratio analysis. Although the respondents who agreed with the statement, "generic substitution will contribute to the reduction in the national medical expenditure" seemed to be more likely to be BR statin users (odds ratio = 0.40, not statistically significant), the respondents who agreed that "generic drugs are less expensive than brand-name drugs" were more likely to be GE statin users (odds ratio = 4.55, $P < 0.01$). These two aspects seem to be somewhat contradictory. However, the former finding is in line with previous findings that patients prefer brand-name drugs compared to generic drugs, even when patients were aware of the value and benefit of generic drugs (Kobayashi et al. 2011; Shrank et al. 2009; Keenum et al. 2012; Sewell et al. 2012). One of the previous authors summarized the patients' attitudes as "generic medications for you, but brand-name medications for me" (Keenum et al. 2012). On the other hand, the latter finding indicates that the respondents who actually realize the lower cost of generic statins and the reduction of their own out-of-pocket money actually seem to prefer generic statins, since the odds ratio (= 4.55) for this view is the largest one among odds ratios of other respondents' views. Therefore, these findings suggest that a certain amount of true reduction in the patients' own out-of-pocket money may encourage the patient to substitute. This is consistent with a previous Japanese study that found that 85% of the patients who requested to use generic drugs indicated the reason to be the reduction of their own out-of-pocket money, and none of them discussed a reduction of medical expenditure (Inoue et al. 2008).

No significant difference was observed in the mean value of the average copayment of pharmacy fee between BR statin users and GE statin users. This finding may be associated with the fact that GE statin users already experienced a certain amount of reduction in their copayment by generic drug substitutions. Although not shown in the results, the estimated mean value of average copayment in GE statin users, in the assumption of BR statins use in place of GE statins, is calculated as 2741.8 JPY (= 25.2 US$), which is not significantly higher, but almost 500 JPY (= 4.6 US$) higher than the real mean values of the average copayment in BR statin users, which is 2155.7 JPY (= 19.8 US$). The difference of 500 JPY (= 4.6 US$) is consistent with the cost saving with regard to the question on how much reduction would encourage respondents to substitute. The respondents first indicated 1000–1999 JPY (= 9.2–18.4 US$) per pharmacy visit, and then 500–999 JPY (= 4.6–9.2 US$) in regard to the question. Simply simulating the difference in the patient's out-of-pocket money in the case of fluvastatin [20 mg tablet (brand-name 62.3 JPY vs generic 37.1 JPY) as a once-daily 20 mg tablet for 90 days], the difference of out-of-pocket money would be 691 JPY (= 6.4 US$) in the case of 30% copayment, and 230 JPY (= 2.1 US$) in the case of 10% copayment. For pravastatin [10 mg tablet (brand-name 84.8 JPY vs generic 33.7 JPY)] in a similar way, the difference in the patient's out-of-pocket money would be 1380 JPY (= 12.7 US$) in the case of 30% copayment, and 460 JPY (= 4.2 US$)in the case of 10%. Thus, patients with a chronic disease whose copayment is 30% should be considered by health-care professionals because they can get a certain amount of reduction in their out-of-pocket money by substituting from brand-name drugs to generic drugs. However, since almost half of Japanese hyperlipidemia patients are over 70 years old (MLHW 2014b), their copayment rate is 10–20%, not 30%. As simulated above, the difference of out-of-pocket money by substitution is not sufficiently large to encourage patients with 10–20% copayment to substitute under the current Japanese drug price policy. Though currently in Japan, the drug price of generic drugs is set generally as 50% of that of a brand-name drugs, a greater difference in the drug price between brand-name drugs and generic drugs is necessary by reducing the prices of generic drugs as a policy. The introduction of a kind of reference pricing system, such as that which has been already introduced in European countries, may be considered as one of the policy options (Giuliani et al. 1998; Brekke et al. 2009; Drozdowska and Hermanowski 2016; Rathe et al. 2013).

Though this study investigated which factors encourage patients to substitute, further study is needed to define whether generic substitution truly contributes to a reduction in medical expenditure without any negative effects on therapy outcomes. Numerous studies have reported on the pros and cons of the effects of substituting or on the use of generic statins with regard to patient adherence and therapy continuation (Slazak et al. 2016; mano et al. 2015; Degli Esposti et al. 2016; O'Brien et al. 2015; Li et al. 2016; Gagne et al. 2014). In a Japanese study, it was reported that changing from brand-name atorvastatin to generic statins did not affect patient adherence (Mano et al. 2015). Another study reported that refill compliance was not negatively affected by a physician-induced switch to generic drugs (Ude et al. 2011). Since the respondents in the present study indicated they did not mind taking generic drugs if their physician prescribed it, our data also provided some evidence that a physician-initiated switch may not negatively affect the patient's therapy outcomes, including patients' adherence.

Limitations of this study are the small sample size and the fact that it was conducted in only one region of Japan. Caution must be taken when deriving consequences from non-statistically significant results, given that there might have been a lack of statistical power (wide confidence intervals) due to a small sample size. Since the generic use share is different among regions in Japan, a greater sample size survey should be conducted in other regions of Japan. This study focused only on statins, lipid-lowering drugs among all of the drugs for chronic diseases. Further study should be conducted on other chronic disease drugs such as antihypertensive drugs. Antibiotics, which are acutely prescribed and whose drug price is relatively expensive, should also be a target of research.

Conclusions

Physician-initiated switching is welcomed by respondents in the present study, which is able to remove their concerns on generic drugs. A policy framework encouraging physicians to write prescriptions for generic drugs may be a powerful tool to lead to patients to switch without concerns.

A much greater difference in drug price between brand-name drugs and generic drugs is necessary; this can be accomplished by reducing the price of generic drugs, which is currently set as 50% of BR price as a policy. The introduction of a type of reference pricing system may be considered as one of the policy options.

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Compliance with ethical standards

Conflict of interest Eriko Kobayashi has no conflict of interest. Chiemi Abe has no conflict of interest. Nobunori Satoh has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Patients' consent to participate was indicated by returning the completed questionnaire.

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