



Price difference as a predictor of the selection between brand name and generic statins in Japan



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ARTICLE INFO

Article history:

Received 27 July 2014

Received in revised form 7 January 2015

Accepted 15 January 2015

Keywords:

Brand name drugs

Generic drugs

Price difference

Claims database

Out-of-hospital pharmacies

Logistic regression analysis

ABSTRACT

Objectives: This study aimed to explore the predictors of the selection between brand name drug (BR) and generic drug (GE) and to clarify the quantitative relationship about selection. **Methods:** We identified “incident users” who dispensed statins between April 2008 and June 2011 in commercially databases consisted of dispensing claims databases (DCD) of out-of-hospital pharmacies and hospital claims databases (HCD) of in-house pharmacies in Japan. Predictors of the selection between BR and GE, including price difference (PD), the price of BR, their interaction and percent change of the price of GE relative to BR were explored by logistic regression using DCD and HCD separately.

Results: We extracted records of 670 patients who have opportunity for selection both BR and GE. Logistic regression analysis demonstrated that PD, the price of BR, interaction between them, and prescriber affiliation were factors significantly associated with the selection in the DCD; $\text{logit}(p) = 9.735 - 0.251 \times \text{PD} - 0.071 \times \text{the price of BR} + 0.002 \times \text{PD} \times \text{the price of BR} - 1.816 \times \text{affiliation} + 0.220 \times \text{gender} - 0.008 \times \text{age} + 0.038 \times \text{monthly medical fee}$. PD was inversely proportional to BR choice in DCD and lead to the opposite result in HCD. Numerical simulation of selection revealed that the quantitative relationships heavily depend on situations.

Conclusions: PD and the price of BR are predictors of the selection between BR and GE interactively in out-of-hospital pharmacies, but not in in-house pharmacies of medical facilities. Results may support policies which increase the power of out-of-hospital pharmacies for selection.

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1. Introduction

It is widely recognized by governments in developed countries that encouraging generic drugs (GEs) instead of brand name drugs (BRs), substitutable drugs with GE, is an appealing policy to reduce medical expenditures. The price of GEs is generally lower than that of BRs, acting as a prescribing incentive for medical facilities, prescribing

physicians, pharmacists and patients. In fact, share of GEs prescribed is over 70% in the US and over 60% in the UK and Germany by quantity based [1–4], but share of GEs in Japan is around 40.0% in 2013 [5].

Several studies in western countries have shown a variety of effects of the entry of GEs [6–11], such as deliver competition [9], decreases in the average drug price in the market [6,10], increases in the price of BRs [7,8], and switching to other in-patent drugs in the same therapeutic class results in an increase of pharmaceutical expenditure [11]. However, encouraging GEs is expected to deliver significant savings to health insurers in general.

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Recently, the total health-care expenditure and medication cost of Japan amounts to 40 trillion yen. Ministry of Health, Labour and Welfare (MHLW) regards encouraging use of GEs as effective measures to control those expenditure [5], and several policies have been implemented since 2001 [12–14], including introduction of a new type prescription form of external prescription in April 2008. This form allow pharmacists in out-of-hospital pharmacies to dispense both BRs and GEs after obtaining patient consent, increasing flexibility in selection between BR and GE [12]. On the other hand, the prescription form of internal prescription did not changed, implying that internal prescription reflects physician's choice [12] (Fig. 1).

Several studies have investigated determinants of the use of GEs. Database studies in Switzerland and Norway revealed that price difference as well as price of BRs was associated with substitution of BRs for GEs [15,16]. In the database studies in Netherlands, Belgian and Australia, characteristics of patients such as acknowledgement of availability of GEs, age, sex, pharmacy status and drug categories showed effects on substitution of GEs [17–19]. A questionnaires study in Portugal also revealed an effect of communication with doctor and pharmacists [20]. However, these previous studies did not discriminate selection between BR and GE at the beginning of administration and in the settings of switching and prescription at in-house pharmacies in medical facilities and at out-of-hospital pharmacies. Moreover, data from Japan is limited particularly at a patient-level [14,21].

This study therefore aimed to explore predictors of the selection between BR and GE. To increase accuracy of the estimated quantitative relationships, we focused on BR and GE of statins rather than heterogeneous drug categories and adopted incident user design, in which patients with the first dispensing are identified and selected as study subjects rather than patients who switched to GE.

2. Methods

2.1. Study design

This is an analysis of a commercially available database of claims from employee's health insurance societies, acquired by the Japan Medical Data Center (JMDC) [22]. Dataset consists of dispensing claims data (DCD) containing information on all drugs in out-of-hospital pharmacies and hospital claims data (HCD) in pharmacies of medical facilities (in-house pharmacies), respectively. Those databases covers eight million claims of employee's health insurance societies and one million people, which account for 0.78% of the population of Japan, and the population is composed of large company (capitalized at five hundred million yen or more in Companies Act in Japan) workers with stable lifetime employment and included their dependent relatives. One advantage of using claims information as administrative data is that it is an almost complete collection of information on diagnostic procedures, treatment, and expenses.

2.2. Conceptual model

We initially identified potential predictors of the selection between BR and GE from interviews with pharmacists and data from previous studies [13,15,16,21,23–29] and created a conceptual model which represents selection between BR and GE (Fig. 1). The conceptual model includes potential predictors of the selection, selectors (patients, pharmacists, and physicians), place of selection, and results of selection. In this model, factors that could not be extracted as variables are indicated in gray shading. Selectors who have a choice BR and GE are indicated white-on-black.

The upper part of the conceptual model shows selection at out-of-hospital pharmacies and reflected in DCD. The lower part shows selection at in-house pharmacies in medical facilities and reflected in HCD. After the introduction of a new prescription form at 2008, in Japan [12], pharmacists at out-of-hospital pharmacies can select BR or GE after obtaining patient consent and physician sign-off to the substitution (drug substitution), but patients and pharmacists do not involved in prescription or selection of BR or GE at in-house pharmacies in medical facilities [12]. We assumed that price difference, the price of BR (medicine price of BR [e.g. “Mevalotin”, for pravastatin] which was compared with GE [e.g. “Mevarich”, for pravastatin] at the place of selection), gender or age, copayment for medical fee, and income were potential factors associated with selection by patients. The incentive of insurance reimbursement related to company business policy, the burden of stock inventory, as well as concern regarding GE product quality and availability could affect selection by the pharmacists. Out-of-hospital pharmacies are usually belonging to chains of pharmacies, because policies and concerns of their front office have a influence on stock, adoption, and selection of GE. Price gap between the reimbursement prices and the wholesale prices are considerable factor, however it is impossible to identify the individual wholesale prices. Prescriber affiliation, customary practice of prescription (including brand loyalty), sales promotions, clinical condition and preference of physicians were potential factors associated with selection by physicians [29]. Meanwhile, prescription form of internal prescription which directly reflects prescription of physicians was without any changes. Pharmacists of in-house pharmacies have no legal right to give an explanation about selecting BR or BR. Besides, previous studies demonstrated that little relationship between physicians' perceptions of patient cost burden and their perceptions of GEs [29].

2.3. Database

DCD included details of medicine dispensed by pharmacists at the out-of-hospital pharmacy, pharmacy identifier, patient information (age, gender, monthly all medical practice fee including initial visit fee, all prescribed drugs, examination, dispensing fee, administration fee, and all that), information on drug dispensed (HOT reference code [standard master for pharmaceutical products], brand name, specifications, GE classification, price, concomitant drug).

HCD included details of medicine dispensed by pharmacist in in-house pharmacies in medical facilities (identifier, department, bed number, classifications of institutions), patients (age, gender, all monthly medical fee including initial visit fee, all prescribed drugs, examination and all that), and information on drug dispensed. We identified prescriber affiliation of these claims data by combination of pharmacy identifier and identifier of medical facilities.

2.4. Subjects

Previous studies in western countries demonstrated that drug categories are related to the frequency of GE substitution [19]. However, given the duration of administration, clinical condition and backgrounds, selection between BR and GE may vary across drug classes. Our target population of inference is therefore statin users rather than the general population. We selected three statins, pravastatin, simvastatin and fluvastatin, as the drug of interest for five reasons: (1) Long-term use of GEs in Japan as standard statin. Almost 5 years have passed from their introducing in 2003; (2) high GEs share as compared to other drug classes (almost 45% in 2012); (3) the sufficient range of price differences in the market as compared to other drug classes; (4) their specific of indication; (5) Similar profiles known as “Mild statins”.

We adopted an incident user design, in which patients with the first prescription are identified and selected as study subjects because inevitably generating opportunities of selecting at the initial administration, unfavorable decision making on newly patients and especially prescribing for hyperlipidemia [30]. We regarded eligible patients as those who were not administered statins between 1 January 2008 and 31 March 2008 and patients administered statins for the first time between 1 April 2008 and 31 June 2011 (Supplement material 1).

2.5. Analysis populations

We defined two analysis populations: the first analysis population was comprised of the “Whole initial statin users” populations who met the eligibility criteria, the second analysis population was “Primary analysis population” after excluding subjects prescribed in pharmacies which did not dispense both BR and GE drugs between 1 April 2008 and 31 June 2011 (Supplementary material 2). This population was used in the primary analysis since only those patients would have opportunity for selection between BR and GE and this dataset reflects patients’ decision more sensitively than the whole initial statin users. These populations include both contents of DCD and HCD. We used DCD for the primary analysis, since selection in out-of-hospital pharmacies would reflect patient intention more directly than in in-house-pharmacies in medical facilities as we stated (Fig. 1).

2.6. Statistical analysis

Patient background characteristics were compared by proportions and Pearson’s χ^2 tests for categorical data, and by mean (standard deviation) and unpaired *t*-tests for

continuous data. Predictors of the selection between BR and GE were explored using multiple logistic regression models. The explanatory variables for the logistic regression models were selected on the basis of the conceptual model; that is, price difference between BR and GE, the price of BR, an interaction term between price difference and the price of BR, patient gender (male = 0, female = 1), affiliation (clinic = 0, hospital including college, national and private = 1), monthly medical fee (as stated in database), and age categories at the time of selection (age from 10 to 69 years were converted into 12 classes by 5 year intervals and 70 years or more was treated as another class). In addition, we examined model included percentage change of price difference (the price of BR minus the price of GE divided by the price of BR) [15].

We therefore examined presence or absence of the interaction term between price difference and the price of BR in these models because models with an interaction term are expected to fit data well even though the true structures are not additive.

We performed sensitivity analyses using models with different sets of covariates including quadratic or interaction terms to examine robustness of the final logistic regression models (Supplementary materials 5 to 10).

To determine the relationship between the price difference and the probability of selection, we performed numerical simulation by inputting parameter values based on scenarios described below into the estimated equation of the multiple logistic regression models. We defined outcomes as initial selection BR or GE in analysis of DCD. In the simulation of selecting BR or GE of 50%, we show results on pravastatin 5 mg and 10 mg with eight scenarios, because pravastatin was the most commonly prescribed drug (not only in Japan but in the database) [31]. All statistical analysis was conducted using SPSS for Windows ver.19 (IBM Corporation, Tokyo, Japan). *P* values < 0.05 were considered statistically significant and all *P*-values were two-sided.

3. Results

3.1. Subject selection

Among 5522 statin users identified in the database, 5078 patients were selected as “Whole initial statin users population” after excluding 444 patients who were not incident users, that is, those who were administered statins between 1 January 2008 and 31 March 2008. After excluding subjects whose pharmacy did not dispense both BR and GE drugs between 1 April 2008 and 31 June 2011, we identified 670 patients who were included in “Primary analysis population” (Supplementary material 2). Those population included contents of DCD and HCD.

3.2. Characteristics of subject

Supplementary material 4 shows the characteristics of subjects among the whole initial statin users population (*n* = 5078). Table 1 shows background of primary analysis population (*n* = 670). The characteristics of these populations were similar. Overall, BR was dispensed to 58.3% of whole statin users (60.5% of the DCD dataset and 56.4% of

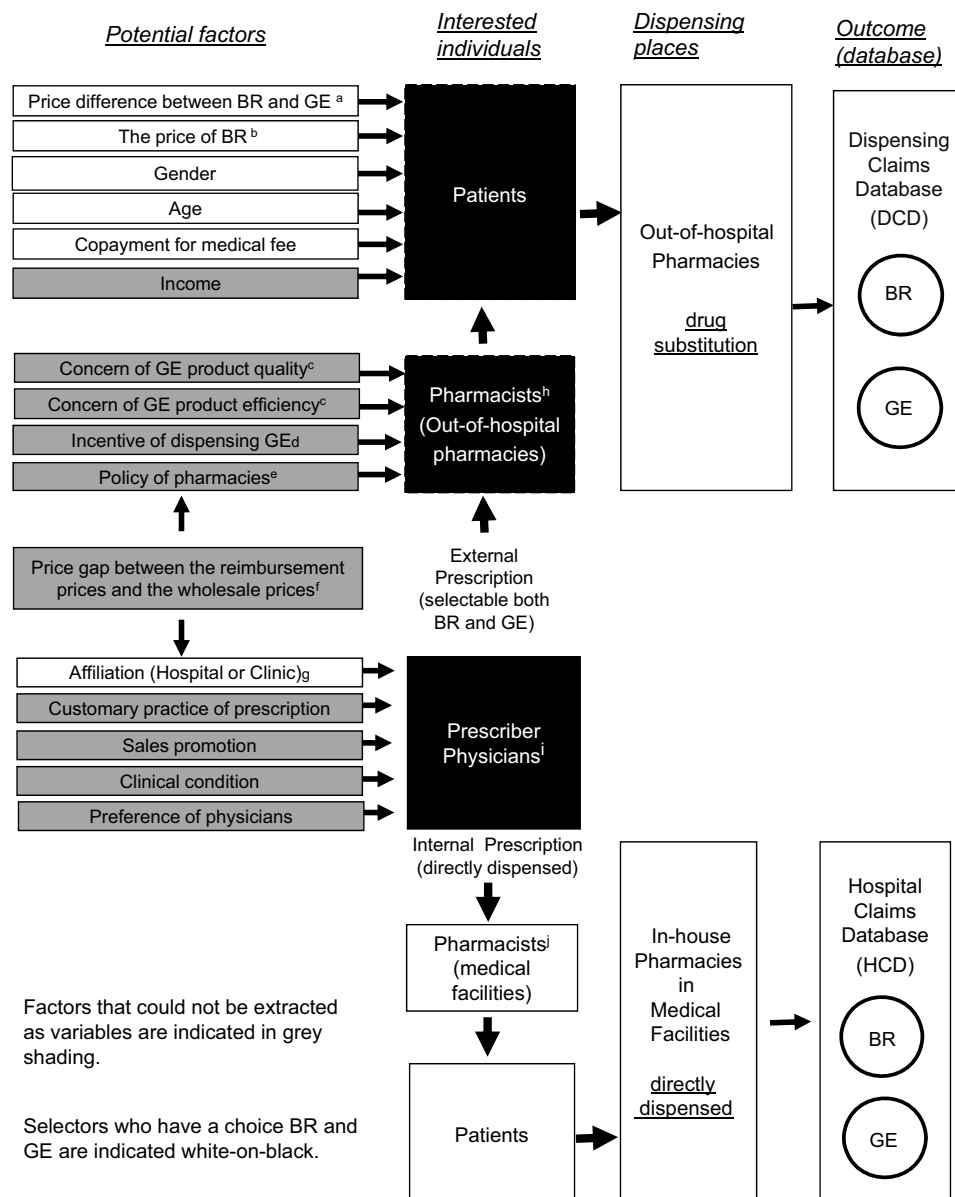


Fig. 1. Conceptual model for selecting brand name and generic drugs. (a) Price difference represents the gap of reimbursement price between BR and GE in Japan. Patients consistently have to pay 10–30% of this price as co-payments. Those who face higher co-payments and when the relative saving is high, they tend to choose a GE [1]. The majority of patients had the correct understanding that GEs are less expensive than BRs [2]. (b) The price of the BR is much higher than that of the former. (c) Clinical equivalence of GE and BR used in cardiovascular disease were demonstrated in a systematic review and meta-analysis [3]. However, the bioequivalence and clinical trials of GE in Japan is quite low [4]. Previous study showed that pharmacists had doubts regarding the reliability of GEs, especially among elderly consumers [2]. (d) MHLW introduced governmental incentives for out-of-hospital pharmacies. In 2008, a new incremental dispensation fee component was introduced. If a pharmacy dispensed at least one generic for 30% or more of its received prescriptions, it was eligible for an incremental dispensation fee [5]. (e) Out-of-hospital pharmacies belonging in the same equation as before a gate of hospitals are usually belonging to chains of pharmacies. Policies of their front office have a impact on stock, adoption and negotiation with distributors. (f) Price gap between the reimbursement prices and the wholesale price are determined when wholesale distributors deliver medicines for out-of-hospital pharmacies and in-house pharmacies (medical facilities). These gaps, which are determined by negotiation with these distributors and regarded as earnings for each pharmacies and facilities are impossible to identify. (g) Affiliation represents type of medical facilities hiring physicians, hospital (including college, national and private) or clinic. Drug formulary at these facilities differ depending on these types. In previous studies, the result of questionnaire survey indicated that physicians engaging in hospital are not particular about the GEs than in clinic in Japan [4]. Another previous study demonstrated that proportion of GEs in clinics are higher than that of in hospitals both quantity and cost base, from insurance claims submitted to the National Health Insurance (NHI) [6]. (h) Pharmacists in out-of-hospital pharmacies have a great influence on choosing, after MHLW introduced a new type prescription form of external prescription in April 2008. This form allow these pharmacists to dispense both BR and GE after obtaining patient consent (drug substitution), increasing flexibility in selection between BR and GE [5]. The default setting of this external prescription is available both BR and GE in out-of-hospital pharmacies. (i) Physicians, who play a central role in the prescription decision, have their individual prescribing habits. Preference of physicians have major impact on the selection. In previous studies, the percentage of patients willing to accept GEs substitution are enhanced by not only

Table 1

Background of the subjects in the primary analysis population.

	Dispensing claims data (DCD)			Hospital claims data (HCD)		
	BR (n = 159)	GE (n = 90)	P value [†]	BR (n = 330)	GE (n = 91)	P value [†]
Sex						
Men	102(63.8%)	54(60.0%)	0.56 [*]	290(87.9%)	70(77.0%)	0.02 [*]
Women	57(36.2%)	36(40.0%)		40(12.1%)	21(23.0%)	
Age						
<50 years	65(40.1%)	34(37.8%)	0.63 [*]	171(51.8%)	54(59.3%)	0.20 [*]
≥50 years	94(59.9%)	56(62.2%)		159(48.2%)	37(40.7%)	
Monthly medical fee (thousand yen, mean(SD))	18.6(11.6)	15.9(8.7)	<0.01 ^{**}	15.7(26.3)	14.1(14.0)	0.04 ^{**}
Affiliation						
Clinics (0 to 19 beds)	105(65.6%)	82(91.1%)	<0.01 [*]	304(92.1%)	80(88.0%)	0.21 [*]
Hospitals (≥20 beds)	54(34.4%)	8(8.9%)		26(7.9%)	11(12.0%)	
Statin formulation						
Pravastatin	147(92.5%)	87(96.7%)		315(95.5%)	81(89.0%)	
Simvastatin	2(1.3%)	1(1.1%)		9(2.7%)	9(9.9%)	
Fluvastatin	10(6.3%)	2(2.2%)		6(1.8%)	1(1.1%)	

BR = brand name drugs, GE = generic drugs, SD = standard deviation.

^{*} Pearson's chi-square test.^{**} Student's t-test.[†] All P values for BR vs. GE.

the HCD dataset, Table 1). Proportions of patients aged 50 years or over and of hospital were significantly higher in BR users than GE users in the DCD, while BR users included more men than GE users in the DCD. Mean monthly medical fee were significantly higher in BR users than GE users in both databases. These results may reflect intention of prescriber physicians of clinics where cost for drugs are valued more than in hospital. Both BR statin and substitutable GE were dispensed at 52 out-of-hospital pharmacies (n = 249) and 29 in-house pharmacies in medical facilities (n = 421) and these patients were selected as the primary analysis population. Dispensing rate of pravastatin were about 94% in statins, which reflects typical out-of-hospital pharmacies and in-house pharmacies in medical facilities in Japan at 2008.

3.3. Factors associated with selection between BR and GE

Table 2 shows the results of multivariate analysis using logistic regression from the DCD of 52 out-of-hospital pharmacies (n = 249; primary analysis) and the HCD of 29 in-house pharmacies in medical facilities (n = 421; secondary analysis), respectively. In the DCD, price difference, the price of BR, an increase in monthly medical fee and affiliation were significantly associated with selection between GE and BR. The interaction between price difference and the price of BR was also significant.

In the HCD, 68% (288/422) of patients received drug dispensed at one particular medical institution, where the selection rate for BR drugs was 89%. The selection probability of GE was significantly higher for women than for men (P < 0.01). Price difference and the price of BR were no longer significant in this dataset.

Supplementary materials 5 to 10 show the results of sensitivity analyses. The quadratic term as well as the linear term of price difference was not significant in DCD if the models did not include the interaction (Supplementary materials 5, 6 and 8) but price difference, the price of BR and their interaction were all significant in adjusted (Supplementary material 7) and unadjusted (Table 2) models. The percent change of the price of GE relative to BR was not significant in the DCD, but was proportional to BR choice in HCD (Supplementary materials 9 and 10).

3.4. Numerical simulation

Fig. 2(a) and (b) shows the relationship between the probability of selecting BR and price difference between BR and GE for pravastatin 5 mg (the price of BR; 59.3 yen) and 10 mg (the price of BR; 112.2 yen), which accounted for 94% of statins in primary analysis population based on the equation in Table 1. We simulated eight scenarios including the interaction between price difference and the price of BR, affiliation (clinic or hospital), sex (man or woman), and age (30 years or 60 years) as shown in the curves. These

pharmacists but physicians [7]. However, previous findings demonstrated that they tend to prescribe by brand name, generally ignoring drug prices [1], and there were little relationships between physicians' perceptions of cost burden and of GE [8]. Another study demonstrated that physicians acknowledge that there may be no problems in taking the BR if a patient does not care about the advantage of cost difference between the BR and the GE in Japan [4]. Besides, sales promotion of BR is provided by makers after the launch. Thus, it is difficult to formulate a priori hypotheses about their influence by previous studies. (j) Pharmacists of in-house pharmacies in medical facilities are belonging to medical facilities, having a role of directly dispensing prescription. The prescription form of internal prescription did not changed after 2008, implying that internal prescription directly reflects physician's choice only [5]. BR = brand name drugs, GE = generic drugs. Factors that could not be extracted as variables are indicated in gray shading. Selectors who have a choice BR and GE are indicated white-on-black.

Table 2

Logistic regression analysis of selection between branded and generic statins at out-of-hospital pharmacies and in-house pharmacies in medical facilities.

Database	Dispensing claims data (DCD)				Hospital claims data (HCD)			
	Odds ratio ^a	95%CI	Regression coefficient	P value	Odds ratio ^a	95%CI	Regression coefficient	P value
Price difference (+1 yen)	0.778	0.641–0.945	−0.251	0.01	1.141	0.994–1.310	0.132	0.06
The price of BR (+1 yen)	0.932	0.875–0.992	−0.071	0.03	0.978	0.938–1.020	−0.022	0.30
Interaction ^{**}	1.002	1.000–1.004	0.002	0.02	0.999	0.998–1.000	−0.001	0.24
Men vs. Women	1.247	0.666–2.334	0.220	0.49	0.412	0.212–0.802	−0.886	<0.01
Age (+5 years)	0.993	0.841–1.171	−0.008	0.93	1.057	0.934–1.196	0.056	0.38
Monthly medical fee (+1000 yen)	1.039	1.007–1.072	0.038	0.02	1.017	0.994–1.040	0.017	0.15
Hospital vs. clinic	0.168	0.070–0.377	−1.816	0.01	0.801	0.322–1.995	−0.222	0.63

Dispensing claims data (DCD) reflect dispensed medicine at out-of-hospital pharmacies ($n=249$).Provided formula: $\text{Logit}(y) = 9.735 - 0.251 \times \text{price difference} - 0.071 \times \text{the price of BR} + 0.002 \times \text{price difference} \times \text{the price of BR} - 1.816 \times \text{affiliations} + 0.220 \times \text{gender} - 0.008 \times \text{age category} + 0.038 \times \text{monthly medical fee}$.Hospital claims data (HCD) reflect dispensed medicine at in-house pharmacies in medical facilities ($n=421$).

BR = Brand name drugs, GE = Generic drugs, CI = Confidence interval.

^a An odds ratio higher than 1 indicates an association with a higher probability of selecting BR.^{**} Interaction between price difference and the price of BR.

curves vary slightly from curve A to curve H. In this analysis, the monthly medical fee was fixed at an average in the dataset. As shown, GE tends to be selected as price difference increases, but when we simulated pravastatin 10 mg, with a larger the price of BR than 5 mg, the impact of the price difference was smaller. These results suggested that both the price of BR and absolute price reduction are associated with selection and the quantitative relationships may heavily depend on situations. We simulated the price difference which balanced the probabilities of selection. The balance point of selection was achieved at a price difference of 31.7–38.7 (yen) for pravastatin 5 mg (the price of BR; 59.3 yen) and at a price difference of 15.0–53.0 (yen) for pravastatin 10 mg (the price of BR; 112.2 yen).

4. Discussion

This analysis of claims database in Japan explored predictors of the selection between BR and GE of statins. Price difference, the price of BR, their interaction, monthly medical fee, and affiliation were associated with selection between BR and GE in DCD. These findings were almost identical to what was observed in the previous study in Switzerland [15], however the quantitative relationships may heavily depend on situations such as out-of-hospital or in-house pharmacies and pravastatin 5 mg or 10 mg.

In Japan, where a universal health-insurance system mainly consists of national health-insurance and employee's health insurance which covers company workers were introduced, MHLW regulates reimbursement prices of drugs and protects patents of BRs. A reimbursement price of a GE is initially set at 70% of the BR price according to a policy of MHLW, creating a price difference between BR and GE. Then, the GE price is revised every 2 years based on the wholesale price determined by a supplier and wholesale distributors [5,12] (Supplementary material 3). The copayments of drugs paid by patients are set at 30% of the reimbursement price for generations still working, at 10% to 30% for the elderly aged 70 or over, and at 20% for children younger than mandatory education.

In many Western countries, price of GE is 50% or lower than that of BR [32,33], whereas price of GE is set at 70%

of that of BR at the time of release in Japanese pricing system. For this reason, price differences are not as large in Japan as in Western countries, although pricing systems vary across countries, leading to GE shares overtaking those of BRs [34,35]. MHLW and Central Social Insurance Medical Council in Japan have decided reforms of the pricing system and the price of GEs at the time of release will be set at 60% of that of BR in 2014.

Our findings, that price difference is a predictors of the selection, support the effectiveness of this policy as well as the introduction of the new type prescription form of external prescription which increase the power of pharmacists in out-of-hospital pharmacies regarding selection with a consciousness of price difference, however, it is impossible to conclude a causal relationship in a cross-section study.

Moreover, we found that predictors of the selection between BR and GE in HCD were different from those in DCD and price difference was not significant in particular. These results are consistent with the previous findings in which there were little relationships between physicians' perceptions of cost burden and their perceptions of GE [13,29]. Thus, trend analysis on the change in the volume of GE would be of worthy of further research.

There are several reasons for the high share of BR of statins in this study. The first reason is the universal health-care system in Japan, where the burden of copayment on patients is only 30% of the medicine price for generations still working. Second, the price of GE at the time of release is 70% of the price of BR, thus reducing the impact of price differences smaller than those in western countries. Third, the datasets used in this study were composed of company workers with stable lifetime employment and included their dependent relatives who are belonging to employee's health insurance societies.

These findings must be interpreted in the context of the limitations of the study. First, we restricted the analysis population for logistic regression to subjects who are expected to have a chance to select BR or GE. However, there were no available information other than the track record of dispensing both BR and GE drugs, only with these data misclassification may occur in terms of the

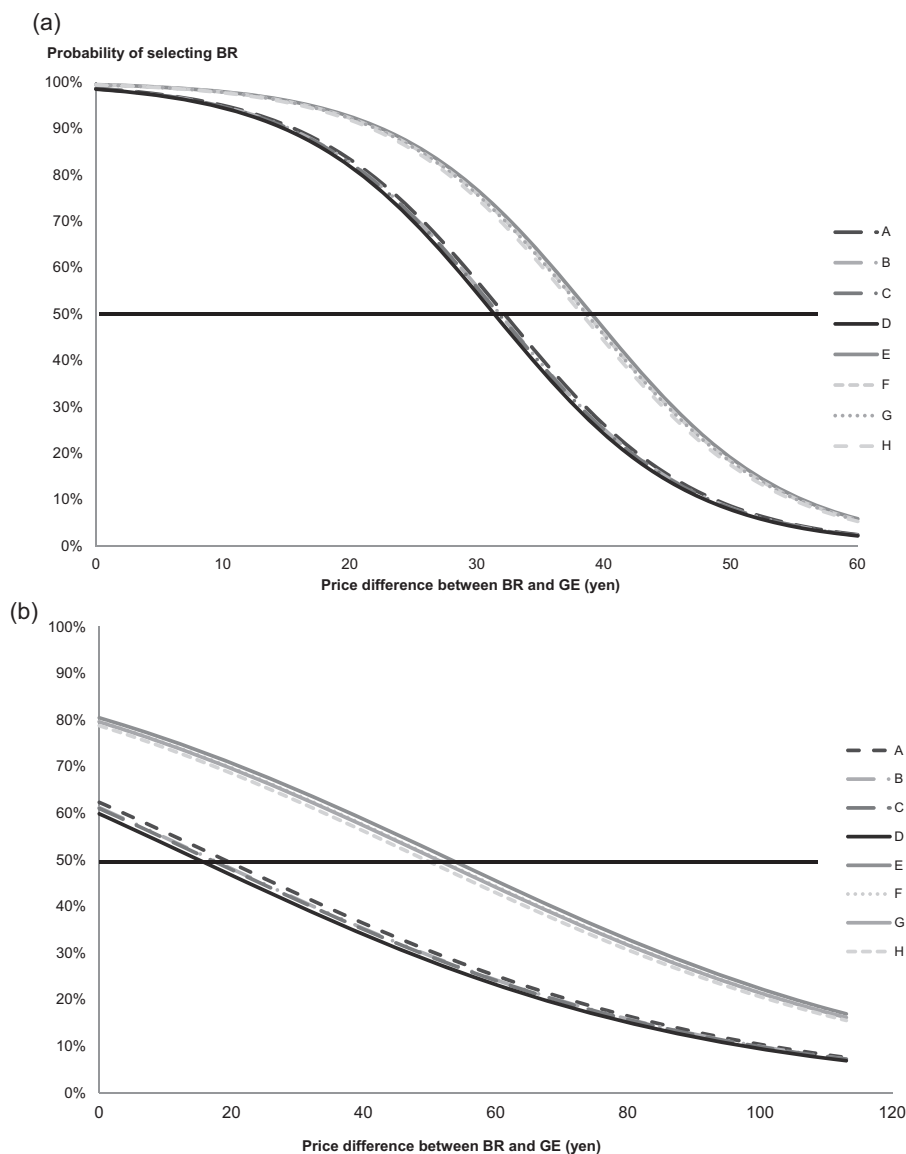


Fig. 2. Numerical simulation. (a) Simulation of the effects of price difference on the selection of brand name statin using the logistic regression model from the dispensing claims data (DCD) (pravastatin 5 mg). (b) Simulation of the effects of price difference on the selection of brand name statin using the logistic regression model from the dispensing claims data (DCD) (pravastatin 10 mg). (a) and 1(b) show the relationship between the probability of selecting BR and price difference between BR and GE for pravastatin 5 mg (the price of BR; 59.3 yen) and 10 mg (the price of BR; 112.2 yen), respectively. We simulated eight scenarios with monthly medical fee fixed. Curve A—affiliation: clinic, gender: male, age: 30 years. Curve B—affiliation: clinic, gender: male, age: 60 years. Curve C—affiliation: clinic, gender: female, age: 30 years. Curve D—affiliation: clinic, gender: female, age: 60 years. Curve E—affiliation: hospital, gender: male, age: 30 years. Curve F—affiliation: hospital, gender: male, age: 60 years. Curve G—affiliation: hospital, gender: female, age: 30 years. Curve H—affiliation: hospital, gender: female, age: 60 years. Selection equilibrium (50%) was achieved at a price difference of 31.7–38.7 (yen) for pravastatin 5 mg and 15.0–53.0 (yen) for pravastatin 10 mg. BR = Brand name drugs, GE = Generic drugs.

identification of out-of-hospital pharmacies and in-house pharmacies in medical facilities which had “actually” provided patients with occasion of selection and dispensed both BR and GE. Second, data on some factors that can be associated with selection were not available, as we indicated in the conceptual model. As we discussed, patient incomes may be higher than the average in this study. But it is difficult to discuss economic incentives and effect of price difference from the point of income.

Another limitation is lack of important covariates, such as income, educational attainment, level of cholesterol, preference of physicians, and health system-specific variables, as indicated by gray color in the conceptual model. Among them, preference of physicians may be more influential than price difference.

Finally, our conclusions may not be generalized to other drug categories or less wealthy population because we focused on statins and the JMD databases. In Japan,

employees' health insurance covers about 29 million people and the JMDC databases include about 1 million people, which account for 3.4%. Thus, our conclusions are not applicable to less wealthy populations.

5. Conclusion

In conclusion, price difference and the price of BR are associated with selection between BR and GE interactively in out-of-hospital pharmacies, but not in-house pharmacies in medical facilities. Together with the numerical simulation, we found that the quantitative relationships may heavily depend on situations such as insurance or in-house pharmacies and pravastatin 5 mg and 10 mg. Our findings may support policies which increase the power of pharmacists in out-of-hospital pharmacies regarding selection between BR and GE, such as introduction of the new type prescription form of external prescription.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.healthpol.2015.01.010>.

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