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Longitudinal Analysis of Generic Substitution

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Abstract Using an extensive longitudinal dataset extracted from the Norwegian Prescription Database (NorPD), Norwegian title: Reseptregisteret, from the Norwegian Institute of Public Health (NIPH) containing all prescriptions written in the period May 2004 to June 2007, we selected two particular drugs (chemical substances) used against cholesterol. The two brand-name products on the Norwegian markets are Provachol (Anatomic Therapeutic Chemical (ATC) classification code C10AA03) and Zocor (ATC code C10AA01). The generics are Provastatine and Simastatine. We find that prices have a negative impact on transitions in the sense that an increase in the brand price will reduce the transition from generics to brand and likewise an increase in the generic price will reduce the transition from brand to generics. Moreover, we find that the older a male doctor is, the more likely it is that he continues to prescribe the brand-name product.

Keywords Generics · Substitution · Microdata · Random utility model · Longitudinal data

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Introduction

In Dalen et al. (2011) we estimated the choice between brand-name and generic drugs based on cross-sectional data. We extracted the entire population of prescriptions in February 2004 and February 2006 on 23 different chemical substances. The observations gave us the choice of on-brand or generics among these patients in these two cross-sections. From the estimated model, we derived price elasticities which were the

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elasticities of the brand products with respect to the brand price. The average of these elasticities was −0.36 in 2004. In the present paper, we exploit the longitudinal dimension of the data and estimate a dynamic model on monthly observations from May 2004 until June 2007 of drug choices for 109 patients in Norway. Our model extends the basic multinomial logit model applied to panel data.[1] It is based on an econometric model developed by Dagsvik (2002). In our model, the current choice depends on all the utility functions associated with each alternative in the past, not only the optimal ones. Thus, we allow for the random parts of the utility functions to be correlated across time and drugs, which implies that taste or habit persistence is included in an otherwise multinomial logit model estimated on panel data. This behavioural assumption implies that individuals' past options, rather than past optimal choices, which would have introduced state dependence in the model, matter for current choices.

From the model we derive transition probabilities that give the transition from brand-name drug to generics and vice versa. We selected only one drug, a drug used against cholesterol, which is the best-selling drug in Norway. The two brand-name products on the Norwegian markets for statins in the period May 2004 to June 2007 were Provachol (Anatomic Therapeutic Chemical (ATC) classification code C10AA03) and Zocor (ATC code C10AA01). The generics are Provastatine and Simastatine. From the model we derived elasticities of the probabilities of shifting from brand to generics with respect to the price of generics and of the probabilities of shifting from generics to brand with respect to the brand price. The average of the elasticities over patients and periods were −0.27 and −0.46 respectively which are not that different from the estimates of the price elasticity derived from the cross-sectional estimates referred to above which also covered not only statins but 22 other substances. In addition to the expected price effects, we found that the older a male doctor is, the more likely it is that he continues to prescribe the brand-name product.

The Norwegian Health System

The Norwegian Health System offers statutory public health insurance. The two drugs considered in this paper are covered by this scheme. Since March 2001, pharmacies are allowed to substitute a branded drug for a generic, independent of the product name prescribed by the doctor. Being permitted to intervene between the physician and the patient, the pharmacies now have an active role in the market for generics. The doctor can still guard against substitution, but this requires an explicit reservation to be added to the prescription note, or "active substitution method". If the doctor refuses to substitute on behalf of a patient who is covered by the social insurance scheme, the brand-name price mark-up, as compared to the cheapest generic version is paid by the social insurance scheme. Even without such a reservation by the physician, the patient may insist on the branded drug, in which case the pharmacy is obligated to hand out the brand-name drug. In this case, the insurance scheme does not cover the price difference between the branded drug and the reference price. The difference has to be paid by the patient.

[1] See for instance Train (2003) and Andreassen et al. (2013).

The Model

We will assume that physicians or patients make a choice of drug type according to what maximizes utility. The model is consistent with consumer theory. In the data we observe the switches between drugs made by the patients. These switches are the observed parallel to transition probabilities and are used to estimate these probabilities. The model accounts for transitions between brand name products and generics.

The model we employ allows for habit persistence and therefore correlation in utilities across time. The inclusion of taste or habit persistence is a behavioural assumption and it implies that agents' past options, not just past optimal choices, matter for current choices. This implies that the current choice depends on all the utility functions associated with each alternative in the past, not only the optimal one.

The model we employ is based on a choice model developed by Dagsvik (2002). Let $U_{nj}(t)$ denote the utility of patient n of using drug j at time t. $j=B$ (brand-name), G (generics). Let C_{nt} be the choice set. We will assume that $\{U_{nj}(t), j \in C_{nt}\}$ is a random utility process. Let $\{v_{nj}(t)+\varepsilon_{nj}(t)\}$ be the period-specific utility in contrast to $U_{nj}(t)$ which are utilities that account for "taste-persistence." The $\varepsilon_{nj}(t)$ are assumed to be independent of $v_{nj}(t)$ and they are assumed to be iid extreme value distributed, that is $\Pr(\varepsilon_{nj}(t) \le x) = \exp(-\exp(x))$.

The model extends the common logit model to deal with correlation in preferences or rather taste persistence. It should be noted that this is not the same as state dependence. With the latter, the choice one has made in the past has a direct impact on the current choices. This is not the case here. The assumption is simply that preferences may be correlated. In Dagsvik (2002) it is shown that:

$$U_{nj}(t) = \max\big(U_{nj}(t-1)-\theta, v_{nj}(t) + \varepsilon_{nj}(t)\big). \tag{1}$$

The coefficient θ may be interpreted as a preference discount factor. If $\theta=0$ there is a complete strong taste persistence, and if $\theta=\infty$ there is no taste persistence at all, and $U_{nj}(t)=v_{nj}(t)+\varepsilon_{nj}(t)$.

Equation (1) means that the time t utility is the max of the two values in the parenthesis. If there is no taste persistence, then the time t utility is the period-specific utility $\{v_{nj}(t)+\varepsilon_{nj}(t)\}$. With taste persistence the time t utility equals $U_{nj}(t-1) -\theta$. It is an empirical question whether there is a significant taste persistence in preferences. The initial time t utility is the period specific utility $\{v_{nj}(0)+\varepsilon_{nj}(0)\}$ when our observation starts, i.e. May 2004. The preferences are random, because as econometricians we do not have a complete and deterministic knowledge of the preferences of the agents. We refer to the textbook by Train (2003) for a discussion of random utility models.

As demonstrated by Resnick and Roy (1990), also Dagsvik (2002), we get a particular autocorrelation function of the utility process in (1):

$$\operatorname{corr}\big\{\exp\big[-U_{nj}(s)\big], \exp\big[-U_{nj}(t)\big]\big\} = e^{\left(v_{nj}(s)-v_{nj}(t)-(t-s)\theta\right)}; \quad \text{for } s \le t. \tag{2}$$

We observe that if covariates are constant over time, the autocorrelation from t to t-1 is approximately equal to $e^{-\theta}$. If $\theta=\infty$, there is no correlation and the model degenerates to a standard multinomial logit model that can be estimated on panel data, (Train 2003).

As shown in Dagsvik (2002) the model can be employed to yield transition probabilities, which in our case will be between brand-name products and generics. The transition probabilities are the following:

Q_{nBGt} probability that agent n transits from brand-name drug in period t-1 to generics in period t

Q_{nBBt} probability that patient n stays on brand-name drug in period t-1 and in period t Q_{nBBt}=1-Q_{nBGt}

Q_{nGBt} probability that patient n transits from generics in period t-1 to brand-name drug in period t

Q_{nGGt} probability that patient n stays on generic in period t-1 and in period t Q_{nBBt}=1-Q_{nGBt}.

The transition probabilities have the following structure:

$$Q_{nBGt} = \frac{\exp(v_{nGt})}{\sum_{r=t_0}^{t} [\exp(-(t-r)\theta_n)][\exp(v_{nGr}) + \exp(v_{nBr})]}; \quad (3)$$

$$Q_{nBBt} = 1-Q_{nBGt} = \frac{\exp(v_{nBt}) + \sum_{r=t_0}^{t-1} [\exp(-(t-r)\theta_n)][\exp(v_{mGr}) + \exp(v_{nBr})]}{\sum_{r=t_0}^{t} [\exp(-(t-r)\theta_n)][\exp(v_{nGr}) + \exp(v_{nBr})]}; \quad (4)$$

$$Q_{nGBt} = \frac{\exp(v_{nBt})}{\sum_{r=t_0}^{t} [\exp(-(t-r)\theta_n)][\exp(v_{nGr}) + \exp(v_{nBr})]}; \quad (5)$$

$$Q_{nGGt} = 1-Q_{nGBt} = \frac{\exp(v_{nGt}) + \sum_{r=t_0}^{t-1} [\exp(-(t-r)\theta_n)][\exp(v_{nGr}) + \exp(v_{nBr})]}{\sum_{r=t_0}^{t} [\exp(-(t-r)\theta_n)][\exp(v_{nGr}) + \exp(v_{nBr})]}. \quad (6)$$

The deterministic part of the period specific utility function, v_{njt}, $j=B,G$, is assumed to depend linearly on observed covariates. Period t_0 is the date of entry of the drug to the market. The variable t_0 is set equal to this date because the data we use are detailed registry data that started in May 2004. The model is estimated by a standard maximum likelihood procedure. The likelihood is:

$$L = \prod_n \prod_t Q_{BGnt}^{y_{nt}} (1-Q_{BGnt})^{1-y_{nt}} Q_{GBnt}^{z_{nt}} (1-Q_{GBnt})^{1-z_{nt}} \quad (7)$$

where y_{nt} and z_{nt} are dummy variables defined as follows:

$$y_{nt} = \left\{ \begin{array}{l} 1 \text{ if transition from Brand to Generic} \\ 0 \text{ otherwise} \end{array} \right\}; \quad (8)$$

$$z_{nt} = \left\{ \begin{array}{l} 1 \text{ if transition from Generic to Brand} \\ 0 \text{ otherwise} \end{array} \right\}. \quad (9)$$

We assume that the deterministic part of the utility function depends on the price of the drug, and of the interaction between age and gender of both patient and doctor. We expect that price has a negative impact on demand. Furthermore, we expect that male patients, in particular when they are getting older, are less likely to make generic substitutions, and that the prescribing doctor is less likely to accept generic substitutions if they are males, in particular when they are getting older. The persistence in choosing brand-name drugs by old male patients and old male doctors is most likely due to conservative preferences. Thus we assume:

$$v_{nGt} = \alpha_G + \beta_1 P_{nGt} \quad (10)$$

$$v_{nBt} = \alpha_B + \beta_1 P_{nBt} + \beta_2 Patient\_age_{nt} x Male_n + \beta_3 Doctor\_age_{nt} x Male_n \quad (11)$$

where P_{nGt} is the price of the generic drug and P_{nBt} is the price of the brand name drug.

Table 1 Descriptive Statistics (number of observations 3898 – 109 patients)

Symbol	Description	Mean	Std.Dev.	Min	Max
	Mean number of prescriptions for statins (May 2004-June 2007)	35.7600	6.3300	28	52
p_ddd	price (in NOK) per daily dose (i.e. p_ddd = no_packages * p_packages/no_ddd)	2.7184	1.9349	0.5679	9.7388
p_not	price of drug not chosen	3.6193	2.1647	0.8693	9.6857
b	Dummy: *b*=1 if brand drug name is equal to "Pravachol" and atc_code is equal to "C10AA03" or drug_name is equal to "Zocor" and atc_code is equal to "C10AA01", *b*=0 if generic (i.e. Provastatine and Simastatine)	0.1637	0.3700	0	1
p_generic	Price per daily dose of generic drug	2.3705	1.1450	0.5679	7.085
p_brand	Price per daily dose of brand drug	3.9671	2.5000	0.8694	9.7388
doctor_age	Age of the doctor	50.5870	9.3071	29	68
patient_age	Age of the patient	78.4250	8.6641	50	91
doctor_female	Dummy: 1 if doctor is female, 0 otherwise	0.1329	0.3395	0	1
doctor_male	Dummy: 1 if doctor is male, 0 otherwise	0.8671	0.3395	0	1
patient_female	Dummy: 1 if patient is female, 0 otherwise	0.4115	0.4922	0	1
patient_male	Dummy: 1 if patient is male, 0 otherwise	0.5885	0.4922	0	1
months	months of drug prescription ranges from 5 (May 2004) to 42 (June 2007)	28.9690	8.6594	5	42

Table 2 Estimates

Variables	Parameters	Estimates	*t*-values
Constant	α	3.2152	15.337
Price	β_1	−1.1913	−2.841
Patient_age × patient_male	β_2	−0.0373	−0.965
Doctor_age × doctor_male	β_3	0.2096	3.967
Preference discount factor	θ	3.7475	4.249
No of observations	3898 (109 patients)		
Log-likelihood	- 433.126		

The prices may vary across time, pharmacies, strength of the drugs, and patients. It should be noted, however, that for all individuals social security covers part of the expenses on statins. The exception is when the patient makes a choice different from what the doctor has prescribed or what the pharmacy will dispense. This is accounted for in the paper.

From the structure of the model we can only identify $\alpha_B - \alpha_G = \alpha$. Our expectation with respect to the signs of the coefficients are $\beta_1 < 0$, $\beta_2 > 0$, $\beta_3 > 0$. The model implies the following price-elasticities:

$$
\begin{array}{lll}
\text{(a)} & El Q_{nBGt}: & P_{nGt} = \beta_1 P_{nGt} Q_{nBBt}; \quad \text{for } t > t_0 \\
\text{(b)} & El Q_{nBBt}: & P_{nGt} = -\beta_1 P_{nGt} Q_{nBGt}; \quad \text{for } t > t_0 \\
\text{(c)} & El Q_{nBGt}: & P_{nBt} = -\beta_1 P_{nBt} Q_{nGBt}; \quad \text{for } t > t_0 \\
\text{(d)} & El Q_{nBBt}: & P_{nBt} = \beta_1 P_{nBt} \dfrac{Q_{nGBt} Q_{nBGt}}{Q_{BBnt}}; \quad \text{for } t > t_0 \\
\text{(e)} & El Q_{nGBt}: & P_{nGt} = -\beta_1 P_{nGt} Q_{nBGt}; \quad \text{for } t > t_0 \\
\text{(f)} & El Q_{nGGt}: & P_{nGt} = \beta_1 P_{nGt} \dfrac{Q_{nGBt} Q_{nBGt}}{Q_{nGGt}}; \quad \text{for } t > t_0 \\
\text{(g)} & El Q_{nGBt}: & P_{nBt} = \beta_1 P_{nBt} Q_{nGGt}; \quad \text{for } t > t_0 \\
\text{(h)} & El Q_{nGGt}: & P_{nGt} = -\beta_1 P_{nBt} Q_{nGBt}; \quad \text{for } t > t_0
\end{array}
\tag{12}
$$

where the elasticities are defined as follows:

a) for transition from brand to generic as a consequence of an increase in generic drug price P_G;

Table 3 Variances, covariances, and correlations of parameter estimates (variances on the diagonal, covariances in the lower triangular part, and correlations in the upper triangular part of the table)

	α	β_1	β_2	β_3	θ
α	0.0439	−0.4540	−0.0030	−0.1180	0.5720
β_1	−0.0398	0.1758	−0.2790	−0.2280	0.1230
β_2	−0.0000	−0.0045	0.0014	−0.3520	−0.0480
β_3	−0.0013	−0.0050	−0.0007	0.0027	−0.0290
θ	0.1057	0.0455	−0.0016	−0.0013	0.7778

Table 4 Elasticities of the transition probabilites with respect to prices; averaged over patients and periods

Variables	Mean	Min	Max	Std. dev.
eq. 12 a) ElQ_{BGnt}: P_G	−0.2732	−0.8416	−0.0658	0.1293
eq. 12 b) ElQ_{BBnt}: P_G	0.0092	0.0006	0.1189	0.0111
eq. 12 c) ElQ_{BGnt}: P_B	0.0101	0.0006	0.1405	0.0142
eq. 12 d) ElQ_{BBnt}: P_B	−0.0003	−0.0008	−0.0001	0.0002
eq. 12 e) ElQ_{GBnt}: P_G	0.0092	0.0006	0.1189	0.0111
eq. 12 f) ElQ_{GGnt}: P_G	−0.0002	−0.0006	0.0000	0.0001
eq. 12 g) ElQ_{GBnt}: P_B	−0.4625	−1.1406	−0.1011	0.2878
eq. 12 h) ElQ_{GGnt}: P_B	0.0101	0.0006	0.1405	0.0142

b) from brand to brand as a consequence of an increase in generic drug price P_G;
c) for transition from brand to generic as a consequence of an increase in brand drug price P_B;
d) from brand to brand as a consequence of an increase in brand drug price P_B;
e) for transition from generic to brand as a consequence of an increase in generic drug price P_G;
f) from generic to generic as a consequence of an increase in generic drug price P_G;
g) for transition from generic to brand as a consequence of an increase in brand drug price P_B;
h) from generic to generic as a consequence of an increase in brand drug price increase P_B;

The Data

The Norwegian Prescription Database (NorPD) was established on January 1, 2004,[2] at the Norwegian Institute of Public Health. The database monitors all drugs that are dispensed by prescription in Norway, and provides information about the patient (age, sex, and insurance status), the physician (age, sex, and speciality), the pharmacy (location), and the dispensed drug (price, package size, strength, product name). Using other sources of information provided by the Norwegian Medicines Control Authority (list of pharmacies and a list of drugs approved for the Norwegian market), we get additional information about pharmacy ownership, identity of the main wholesaler, producer name and price of the drugs. The latter is used to identify brand-name drugs and generics.

In the data set, only the price of the drug chosen (*p_dd*) is reported that may be brand or generic. To generate the price of the drug not chosen (*p_not*) we have done as follows. First we generated a dummy variable (*b_choice*) that identifies if the drug is brand or generic. It equals 1 if the drug name is Pravachol or Zocor (alone or in combination), ATC_code is C10AA03 or C10AA001, 0 otherwise. Then, we generated the mean price (*p_ddd*) over the chosen drug that has same ATC_code, same strength

[2] See Furu (2001)

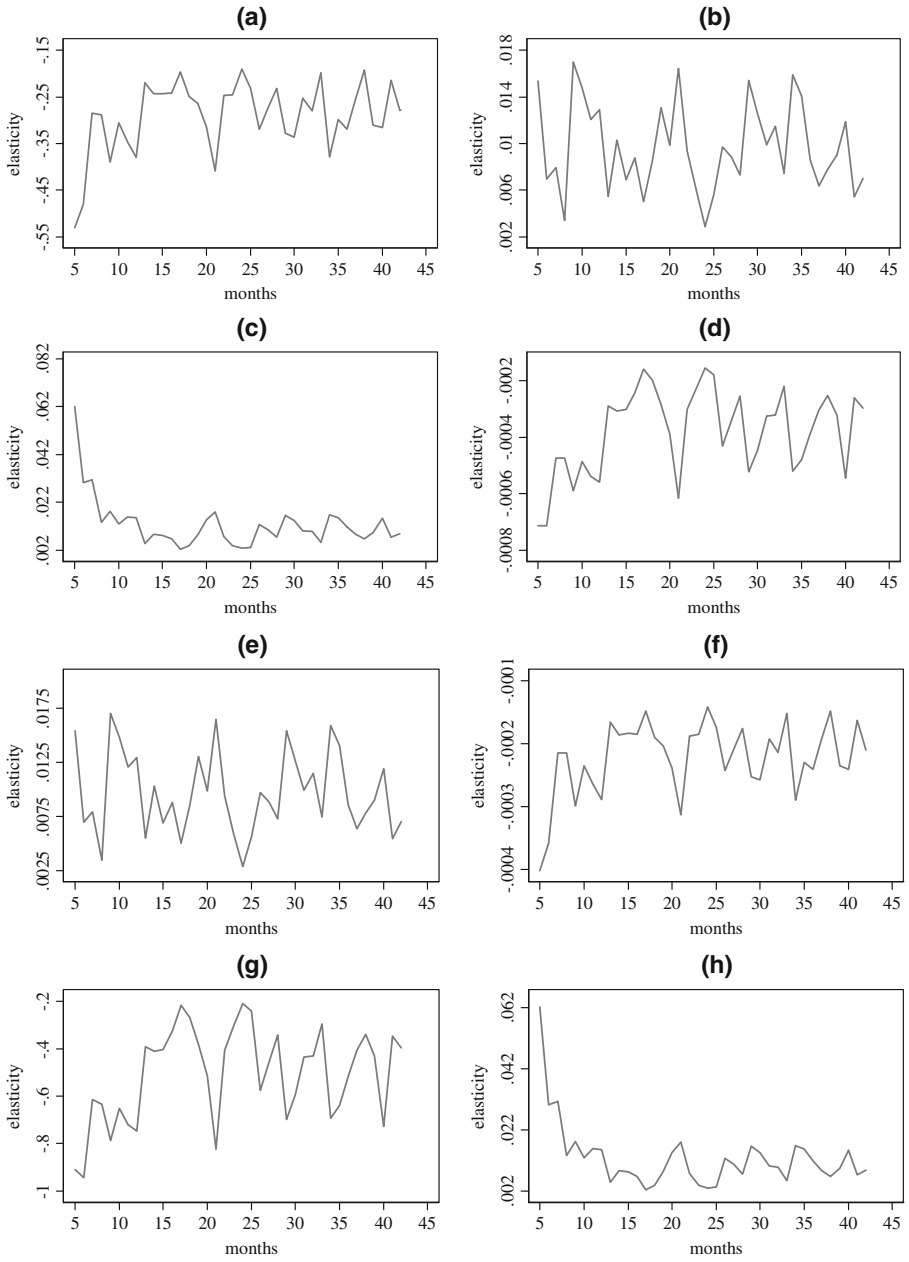

Fig. 1 Mean elasticity of probability vs. month. *Notes*: **a** transition from brand to generic as a consequence of an increase in generic drug price *PG* (eq. 12 a); **b** brand to brand as a consequence of an increase in generic drug price *PG* (eq. 12 b); **c** for transition from brand to generic as a consequence of an increase in brand drug price *PB* (eq. 12 c); **d** from brand to brand as a consequence of an increase in brand drug price *PB* (eq. 12 d); **e** for transition from generic to brand as a consequence of an increase in generic drug price *PG* (eq. 12 e); **f** from generic to generic as a consequence of an increase in generic drug price *PG* (eq. 12 f); **g** for transition from generic to brand as a consequence of an increase in brand drug price *PB* (eq. 12 g); **h** from generic to generic as a consequence of an increase in brand drug price increase *PB* (eq. 12 h)

(*strength*), same pharmacy identifier (*id_n_ph*) and same date of transaction (*months*). At last we generated the alternative price (*p_not*) equal to the mean price just computed, conditioned on *b_choice* (1 or 0). It happens that there are groups in which only brand is chosen or only generic is chosen. In these cases we could not compute the alternative price and we then set *p_not* equal to missing. It also happens that in some groups there is just only one observation useful to compute the average. Also in this case, we set the value of *p_not* to missing. To sum up:

$$p\_generic = p\_ddd*(1-b\_choice) + p\_not*b\_choice;$$
$$p\_brand = p\_ddd*b\_choice + p\_not*(1-b\_choice);$$

where *p_generic* is the price of the generic drug, *p_brand* is the price of the brand drug, *p_ddd* is the price of the chosen drug and *p_not* is the price of the drug not chosen, and *b_choice* is a dummy variable equal to 1 if brand is chosen and 0 otherwise.

In the sample there, are at least 28 prescriptions by patients over the 37 months. We observe drug prescriptions from May 2004, first prescription considered, to June 2007, month five to 42, a total of 37 months. After the selections listed above, we get 3898 observations that refer to 109 patients. The panel is unbalanced since for each patient there are a different number of prescriptions from May 2004 to June 2007.

The descriptive statistics are reported in Table 1. The values reported in the first row show that at minimum a patient has 28 prescriptions, and at maximum 52 prescriptions. The number of prescriptions by patient is not equal to the number of months since there may be more than one prescription per month.

Results

Table 2 gives the estimates and Table 3 gives information on variances, covariances and correlation of the estimated parameters. We observe that price has the expected negative impact on demand and the impact is significant different from zero. The interaction of male doctor and age has a positive and significant impact on the use of brand products. Patient age interacted with gender has no significant impact. The preference discount factor (θ) is positive and significant indicating that preferences are correlated over time, given the covariates in the deterministic part of the utility function.

From Table 4 we observe that all elasticites have the expected sign, which of course is due to the fact that $\beta_1 < 0$. The two sizeable elasticities are the most important ones. The elasticity of transiting from brand to generics (statins) with respect to the generic price is on average equal to −0.2732. The elasticity of transiting from generics to brand (statins) with respect to the brand price is on average equal to −0.4625. The brand price has thus a stronger impact on the transitions than the generic price.

Table 5 Mean correlation of utilities for the 109 patients

corr(exp($-U_{nj}(t-1)$),exp($-U_{ni}(t)$))	Mean	Std. Dev.	Min	Max
$j=B$, $i=B$	0.0234	0.0007	0.0223	0.0260
$j=G$, $i=G$	0.0234	0.0007	0.0220	0.0260
$j=B$, $i=G$	0.2776	0.1258	0.1304	0.8622

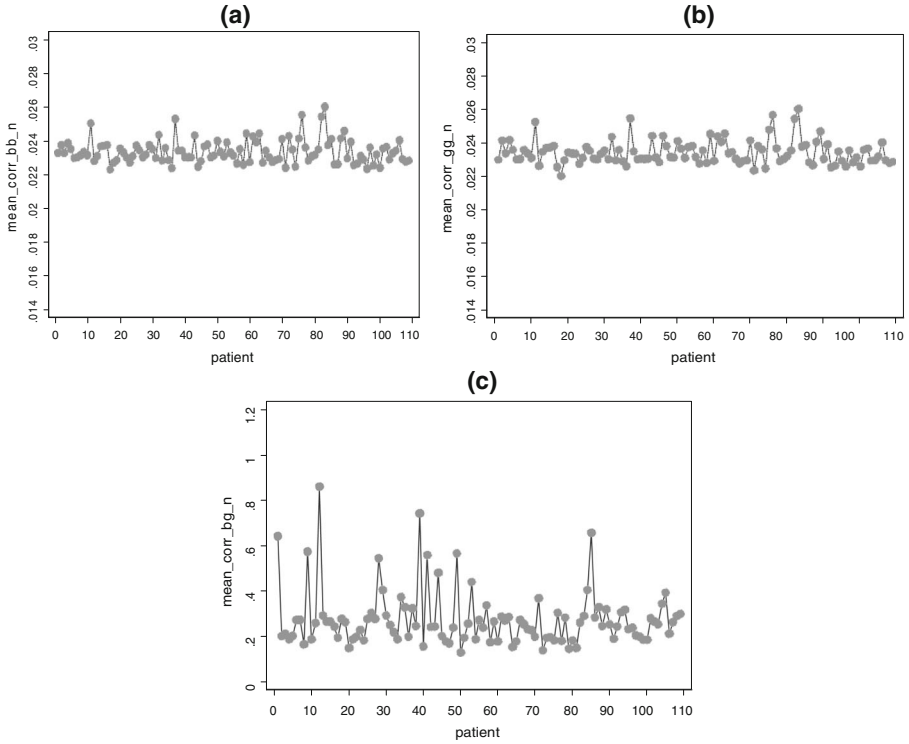

Fig. 2 Mean correlation of utilities: **a** mean correlation of transition from brand to brand, **b** mean correlation of transition from generic to generic, **c** mean correlation of transition from brand to generic

In Fig. 1 we show how elasticities vary across the 37 months. We observe that the two most important elasticities referred to above indicate that price responses were strongest at the beginning of the period (May 2004) and at around month 20 (January 2006).

In Table 5 we report the mean of the correlation of utilites across patients (and time). When the drug type is the same, the correlation is mainly due to the coefficient θ, the preference discount factor. When the drug types are different (*B* and *G*) the correlation is also affected by the fact that the characteristics of the different drug types differ. Figure 2 gives the variation across all 109 patients. Table 6 reports the same correlation across time and Fig. 3 shows how these correlations varied over the 37 months.

Table 6 Mean correlation of utilities across time

corr(exp(−$U_{nj}(t-1)$),exp(−$U_{ni}(t)$))	Mean	Std. Dev.	Min	Max
$j=B$, $i=B$	0.0218	0.0035	0.0118	0.02524
$j=G$, $i=G$	0.0219	0.0034	0.0118	0.0253
$j=B$, $i=G$	0.2536	0.0523	0.0942	0.3145

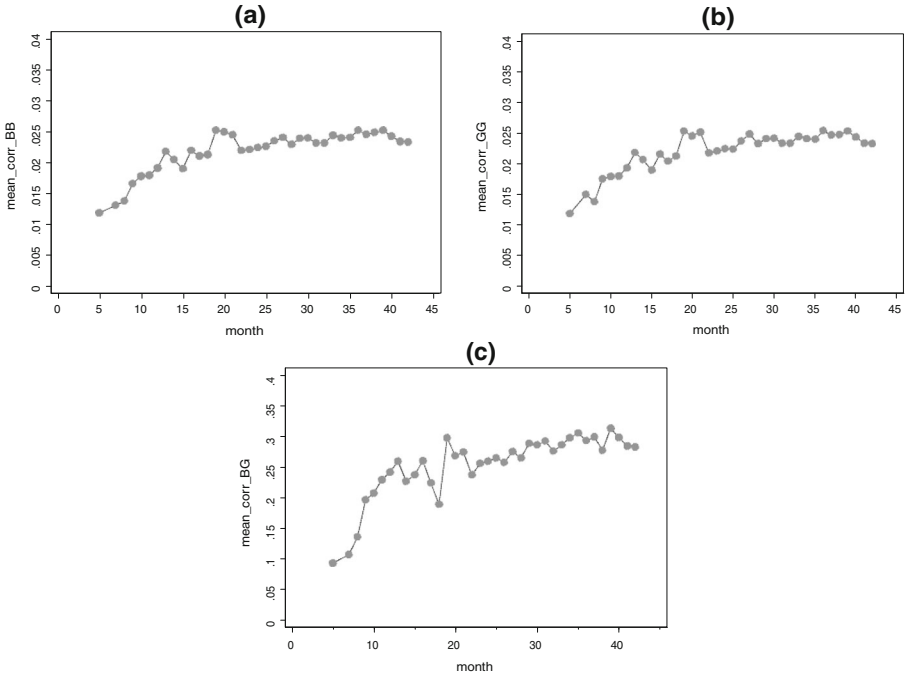

Fig. 3 Mean correlation of utilities across time: **a** mean correlation of transition from brand to brand, **b** mean correlation of transition from generic to generic, **c** mean correlation of transition from brand to generic

Conclusions

Using an extensive longitudinal dataset extracted from the NorPD we extracted information regarding brand and generic drugs against cholesterol (which is one of the most sold drugs in Norway) to derive transition probabilities and elasticities that give the transition from brand-name drug to generic and vice versa. Our model extends the basic multinomial logit model applied to panel data,[3] and it allows for the random parts of the utility functions to be correlated across time and drugs, which implies that taste or habit persistence is included. The estimates implies that habit persistence has a significant impact on preferences.

We find that prices have a negative impact on transitions in the sense that an increase in the brand price will reduce the transition from generic to brand and likewise an increase in the generic price will reduce the transition from brand to generic. The brand price has a stronger impact on the transitions than the generic price. Moreover, we find that the older a male doctor is, the more likely it is that he continues to prescribe the brand-name product.

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[3] See for instance Train (2003) and Andreassen et al. (2013).

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