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ORIGINAL RESEARCH ARTICLE

Multilevel Analysis of the Influence of Patients' and General Practitioners' Characteristics on Patented Versus Multiple-Sourced Statin Prescribing in France

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Abstract

Background The French National Health Insurance and the Ministry of Health have introduced multiple reforms in recent years to increase prescribing efficiency. These include guidelines, academic detailing, financial incentives for the prescribing and dispensing of generics drugs as well as a voluntary pay-for-performance programme. However, the quality and efficiency of prescribing could be enhanced potentially if there was better understanding of the dynamics of prescribing behaviour in France.

Objective To analyse the patient and general practitioner characteristics that influence patented versus multiple-sourced statin prescribing in France.

Methodology Statistical analysis was performed on the statin prescribing habits from 341 general practitioners (GPs) that were included in the IMS-Health Permanent Survey on Medical Prescription in France, which was conducted between 2009 and 2010 and involved 14,360 patients. Patient characteristics included their age and gender as well as five medical profiles that were constructed from the diagnoses obtained during consultations. These were (1) disorders of lipoprotein metabolism, (2) heart disease, (3) diabetes, (4) complex profiles and (5) profiles based on other diagnoses. Physician characteristics included their age, gender, solo or group practice, weekly workload and payment scheme.

Results Patient age had a statistically significant impact on statin prescribing for patients in profile 1 (disorders of lipoprotein metabolism) and profile 3 (complex profiles) with a greater number of patented statins being prescribed for the youngest patients. For instance, patients older than 76 years with a complex profile were prescribed fewer patented statins than patients aged 68–76 years old with the same medical profile (coefficient: -0.225; $p = 0.0008$). By contrast, regardless of the patient's age, the medical profile did not affect the probability of prescribing a patented statin except in young patients with heart diseases who were prescribed a greater number of patented statins (coefficient: 0.3992; $p = 0.0007$). Prescribing was also statistically influenced by physician features, e.g., older male physicians were more likely to prescribe patented statins (coefficient: 0.245; $p = 0.0417$) and GPs practicing in groups were more likely to prescribe multiple sourced statins (coefficient: -0.178; $p = 0.0338$), which is an important finding of the study. GPs with a lower workload prescribed a greater number of patented statins.

Conclusion There is significant variability in the prescribing of different statins among patient and physician profiles as well as between solo and group practices. Consequently, there are opportunities to target demand-side measures to

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enhance the prescribing of multiple-sourced statins. Further studies are warranted, in particular in other therapeutic classes, to provide a counter-balance to the considerable marketing activities of pharmaceutical companies.

Key Points for Decision Makers

- There is significant variability in the prescribing of different statins depending on patient and physician profiles.
- Younger patients with lipid disorders or complex profiles and patients with heart disease are more often prescribed patented statins.
- Older male physicians and GPs in solo practices are more likely to prescribe patented statins.
- There are opportunities to target demand-side measures to enhance the prescribing of multiple-sourced statins.

1 Introduction

Physician prescribing habits and what influences these habits have been extensively evaluated. This interest is in part due to a growth in pharmaceutical expenditure among European countries, with the expenditure outstripping other components of ambulatory care in recent years [1–6]. Unless addressed, this growth will continue and will be driven by well-known factors such as changing demographics, rising patient expectations and the introduction of new, expensive medications [4, 5, 7].

This continued growth in expenditure, as well as its potential consequences on financing comprehensive and equitable healthcare, has resulted in the establishment of multiple supply and demand-side reforms. Supply-side measures for existing drugs include compulsory price cuts as well as initiatives to obtain lower prices for generics, including reference pricing and prescriptive pricing policies [1–3, 8–13]. Demand-side measures include guidelines, an enhanced role for Drug and Therapeutics Committees, academic detailing, continuous medical education that includes quality circles and pharmacotherapeutic groups, access to computerised prescribing tools, benchmarking of prescribing habits, prescribing targets, financial incentives for all key stakeholder groups and prescribing restrictions [1–6, 8–22]. Educational outreach visits have consistently provided small improvements in prescribing, with an increase of 15 % in a desired behaviour seen as a realistic expectation [23–25].

France is no exception, as the National Health Insurance and Ministry of Health have introduced a range of reforms in recent years [1]. These reforms include measures to enhance the prescribing and dispensing of generics by using a combination of educational initiatives, engineering (quality and efficiency targets) and financial incentives [26]. The measures that have been applied are summarised in Box 1 [1, 4, 5, 27]. The various demand-side measures for generics in France combined with a prescriptive pricing policy for generics, with prices 55 % below the originator and reducing further by 7 % after 18 months, led to annual savings for generics estimated at €1 billion in 2009 and €1.3 billion in 2010 for National Public Health Insurance [27, 28].

Box 1 Measures in France to enhance the prescribing and dispensing of generics from 1999 to the present

Educational:
- Government/ National Health Insurance promotional campaigns to enhance the acceptance of generics (since 1999) and INN (International Non-proprietary Name) prescribing (since 2002)
- French Agency for the Safety of Health Products (http://ansm.sante.fr/) regularly provides a list of available generics to ambulatory care physicians
- Since 2004 Health Insurance medical representatives and practitioners have undertaken academic detailing by providing feedback to ambulatory care physicians on their generic prescribing rates benchmarked against local colleagues
- National Health Insurance Agency promoting generics and publishing advertisements on the back of reimbursement forms sent to patients
- National Health Insurance representatives visiting pharmacists to enhance substitution rates where they are low compared to their counterparts (since 2004)

Engineering activities
- National Health Insurance determining annual substitution targets for community pharmacists (generics in place of originators) at the national level as an amendment to the national agreement between community pharmacists and the National Health Insurance Agency
- In April 2010, substitution targets for each regional territory in France were introduced in addition to nationally agreed targets to further enhance substitution

Economic
- Pharmacists guaranteed the same absolute margin for dispensing generic and originator medicines, as well as for potentially negotiating higher prices for dispensing generics to enhance their fees since 2008
- Patients must pay the whole price of a drug themselves if they do not accept generic substitution (since 2009) and subsequently claim the reimbursed cost back from the National Health Insurance. Otherwise, pharmacists cover the National Health Insurance component themselves and claim this back themselves

Voluntary Pay-for-Performance (P4P) pilot schemes were recently introduced in France in 2009 to further improve the quality and efficiency of prescribing [1]. Quality targets include those for vaccinations and drug therapies for chronic diseases, with efficiency targets aimed at increasing the prescribing of generics in a class or related class, including a 70 % prescription target for generic statins [29, 30]. The P4P programme provided €2,800 per GP (about 4 % of the average annual income of GPs) for efficient prescribing [29]. Preliminary analysis of the nationwide pilot P4P programme, which included 40 % of all GPs in France, showed that physicians changed their behaviour towards the recommended prescribing guidelines and targets. As a result, the programme has now been extended to all GPs in France since the end of 2011 [29].

Despite these measures, there was an increase in the prescribing of patented statins in France even after the availability of generic simvastatin [4, 5], resulting in patent-protected statins (atorvastatin and rosuvastatin) representing nearly 60 % of statin prescriptions in 2011 despite numerous studies showing therapeutic equivalence for the statins [31–34] (Fig. 1). This increased prescribing of patent-protected statins resulted in higher prescribing costs for this class in France compared to countries with more intensive demand-side measures to enhance the prescribing of multi-sourced statins [4, 5, 35, 36]. Consequently, additional activities may be needed to further enhance prescribing efficiency in France that take into account the heterogeneity among GPs [37].

Previous studies have shown that younger physicians are more likely to prescribe in accordance with best practice [38], whilst others have demonstrated that physicians' workloads may influence prescribing habits [39, 40]. Furthermore, it has been shown in France that physicians from sector 2 (those GPs that are allowed to charge higher fees than GPs in sector 1) prescribe fewer drugs and for lower costs than physicians from sector 1 [37]. Additional studies have demonstrated that group practices provide higher quality of preventive care compared to solo practices [41]. However, studies focussing specifically on the impact of organisational structure on prescriptions have been very scarce [42], and this impact needs to be further evaluated.

Thus, the aim of this study is to determine the extent of variability among GPs in France in prescribing different statins, i.e., multiple-sourced versus patented statins. The underlying hypothesis is that most variability in prescribing patterns could be explained by differences in physician and patient characteristics.

2 Data and Methodology

We analysed data from the 2009–2010 IMS-Health Permanent Survey on Medical Prescriptions among ambulatory

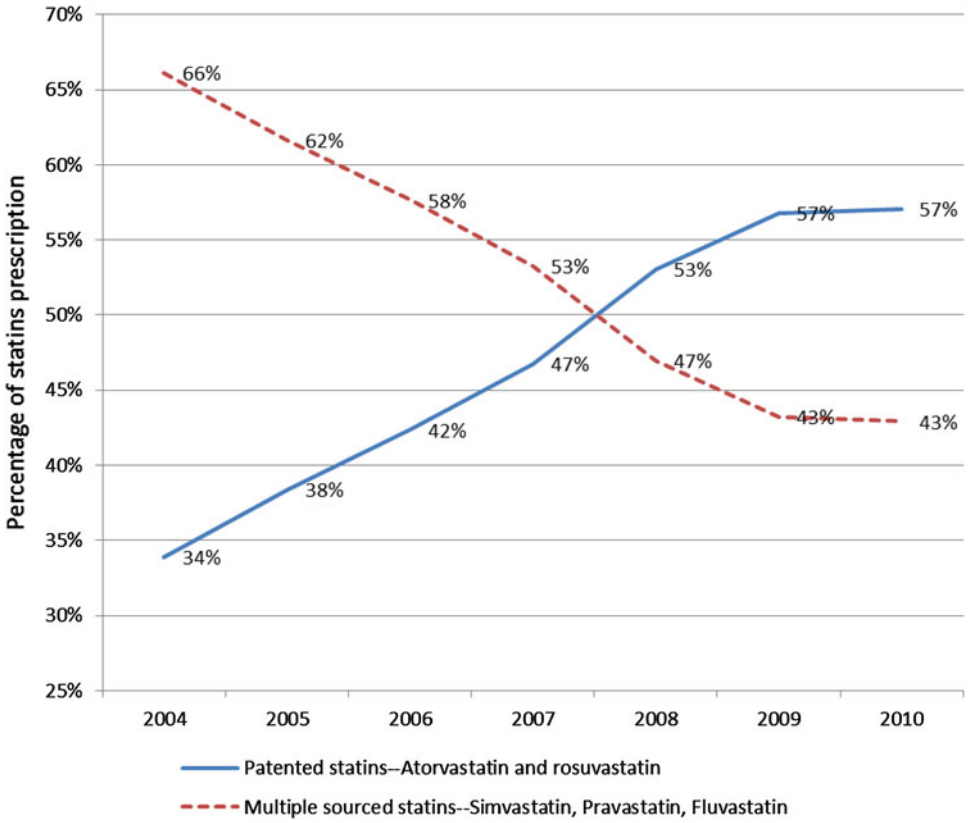

Fig. 1 The evolution of statin prescriptions in France from 2004 to 2011. Source: Institute for Research and Information in Health Economics (IRDES). Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2004–2010

care physicians [43, 44]. This survey provides data on both patient and physician characteristics, which could help explain differences in statin prescribing behaviour. Patient characteristics included age, gender and the diagnosis associated with the visit. Physician characteristics included age, gender, whether they work in a solo or group practice in ambulatory care, weekly physician workload (number of consultations) and fee sector.

2.1 Database

The IMS-Health database contains information on pharmaceuticals that are prescribed by physicians in France as well as the diagnoses associated with these prescriptions each time a new prescription is issued. Each quarter, approximately 850 French general practitioners and physicians (cardiologists, dermatologists, gastroenterologists, gynaecologists, neurologists, ophthalmologists, ENT specialists, paediatricians, lung specialists, rheumatologists and endocrinologists) are asked by IMS-Health to complete a questionnaire concerning all of their patients' visits over a period of 7 days. Surgeons, anaesthesiologists, radiologists, homeopathists, acupuncturists are excluded from the sample as well as ambulatory care physicians that do not prescribe drugs in over 25 % of their visits. The physician sample is partially refreshed each quarter [43] with approximately 15 % of the physicians being excluded from the sample and replaced with new physicians.

Prescription data for GPs only were pooled for 2009–2010. Only visits with at least one prescription of a statin were included in the initial sample, which consisted of 19,121 statin prescriptions by 905 GPs (Table 1). At the time of the study, atorvastatin and rosuvastatin were patent protected in France, whilst simvastatin, fluvastatin and pravastatin were available via multiple sources.

In the initial sample, each GP had on average 6.5 statin prescriptions per week, with a minimum of 1 and a maximum of 34 prescriptions. Because a multilevel model was chosen to analyse the impact of both patient and physician characteristics on subsequent prescriptions, it was believed necessary to fix a minimum level on the number of statin prescriptions per physician. Following established guidance [45], that a minimum of 20 observations is needed at level one for a multi-level analysis, we selected physicians with at least 20 statin prescriptions in their prescription documentation. Thus, we evaluated 14,360 statin prescriptions provided by 341 GPs (Table 1).

In our final sample, 81 % of the physicians were men and 19 % women versus 73 % of the physicians being male and 27 % female in the initial sample.

Physicians were divided into four quartiles depending on their age (Table 2), and physicians' workloads were separated into four parts as well, ranging from lower to higher workloads.

In the database, 327 physicians were from sector 1 where fees are fixed by the national public Health Insurance, whereas only 14 were from sector 2, where physicians are allowed to charge higher fees. Finally, most GPs were either in solo practices (44 %) or in groups with other GPs (32 %) (Table 2).

In total, 53.5 % of patients in the sample were men and 46.5 % were women (Table 3). Their ages were divided into four equally sized classes in order to test the impact of patient ages on the prescription of patented versus multiple-sourced statins. The underlying hypothesis was that the pattern of statin prescriptions will change with patient age similarly to the results of previously reported studies [46]. In our sample, the average patient age in the database was 67 years.

Even if all patients are prescribed statins, their prescriptions may differ depending on their morbidity and comorbidity corresponding to the recommendations set forth by the French National Authority for Health (Haute Autorité de Santé, HAS) [35]. To test the influence of the diagnoses on prescribing patent-protected statins, we designed a classification system based on five medical profiles (Table 3):

- Profile 1: Patients with a single diagnosis of "Disorders of lipoprotein metabolism and other lipidemias" (ICD-10 code E78).
- Profile 2: Patients suffering from any type of heart disease (ICD codes I10 to I15).

Table 1 Statin prescription sample—the number of statin prescriptions for each GP

	Number of GPs	Total number of statin prescriptions	Average statin prescriptions per GP and per week	SD	Minimum per GP and per week	Maximum per GP and per week
Initial sample (minimum of 1 statin prescription per GP)	905	19,121	6.5	4.9	1	33.7
Final sample (minimum of 20 statin prescriptions per GP)	341	14,360	9.1	5.5	2.5	33.7

Source: Institute for Research and Information in Health Economics IRDES

Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2009–2010

Table 2 Descriptive statistics for GP variables for analysis with and without a filter (only GPs with at least 20 statin prescriptions)

Variable		Without a filter % ($N = 905$)	Filter (20 prescriptions) % ($N = 341$)	Statistically significant (S/NS)
Physician's gender	Male	73	81	S
	Female	27	19	S
Physician's age	46 years and under	26.4	23.5	S
	47–51 years	26.1	23.8	S
	52–57 years	26.4	27.9	S
	Over 57 years	21.1	24.9	S
Physician's workload	69 consultations/week and under	39.2	26.7	S
	70–88 consultations/week	23.7	22.9	S
	89–111 consultations/week	19.1	25.5	S
	>111 consultations/week	18	24.9	S
Physician's sector	Fixed fees	94	96	NS
	Extra fees	6	4	NS
Solo versus group practice	GP solo	47	44	NS
	GP combining private practice and hospital activity	15	13.5	NS
	GP in a group practice with other GPs	27	32.3	S
	GP combining private practice and hospital activity in a group practice with other medical specialists	8	8.2	NS
	GP in a group practice with several medical specialists	1.9	2.0	NS

Source: Institute for Research and Information in Health Economics (IRDES)

Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2009–2010

Table 3 Descriptive statistics for patient variables for analysis with and without a filter (only GPs with at least 20 statin prescriptions)

Variable		Without a filter % ($N = 19.121$)	Filter (20 prescriptions) % ($N = 14.360$)	Statistically significant (S/NS)
Patient age	58 years and under	25	24.4	NS
	59–67 years	25.4	25.5	NS
	68–76 years	25.1	24.9	NS
	over 76 years	24.4	25.2	NS
Patient's medical profile	Profile 1 (dyslipidemia)	18.7	17.6	NS
	Profile 2 (heart disease)	20.5	21.1	NS
	Profile 3 (combination of profiles 1, 2 and 4)	53.3	54.6	NS
	Profile 4 (diabetes)	2.9	2.8	NS
	Profile 5 (other)	4.7	3.9	NS
Patient gender	Male	53.5	53.5	NS
	Female	46.5	46.5	NS

Source: Institute for Research and Information in Health Economics (IRDES)

Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2009–2010

- Profile 3: Patients with a diagnosis of dyslipidemia (ICD-10 code E78) associated with heart disease and/or diabetes.
- Profile 4: Patients suffering from diabetes (ICD codes E10 to E14).
- Profile 5: Patients with other diagnoses.

Patients with profile 3 were considered to have a more complex disease than patients with profiles 1, 2 or 4. Consequently, it was expected that prescription patterns would differ depending on patients' diagnostic profiles.

2.2 Method Used to Calculate the Probabilities of a Prescription for Patented Statins

The model used was based on the assumption that π_{ij} represents the probability that a patient is prescribed a patented statin at the ith visit by the jth GP. By using the logistic link function, the general form is:

$$\log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right) = +\beta_{0j}\sum_{k}\beta_{kj}\cdot X_k + \varepsilon_{ij}\,(\text{visit patient}) \quad (1)$$

$$\begin{cases} \beta_{0j} = \gamma_{00} + \sum_{h}\gamma_{0h}.Z_h + u_{0j} \\ \beta_{kj} = \gamma_{k0} + \sum_{h}\gamma_{kh}.Z_h + u_{kj,\forall k} \end{cases} (\text{physician}) \quad (2)$$

We used a multi-level model to analyse the variability in prescribing patented statins as this variability could be attributable to both the patient and physician characteristics [47, 48].

To justify the use of a multi-level model, it was necessary to test the existence of an inter-physician variation of medical practice. This step was performed while estimating a simple null model only with β_{0j}—the conditional mean of the realisation of the event "still patent-protected statin prescription"—which could be divided into in a constant term specific to the GP (γ_{00}) and an inter-physician random effect (u_{0j}) plus the individual residual (ε_{ij}). The estimated variance of the inter-physician random effect (0.548) was significantly different from 0, which justified implementing a multi-level model.

Patient characteristics X_k (age, gender, medical profile) and physician characteristics Z_h (age, gender, solo versus group practice, and physician's workload) were introduced into the model. γ_{k0} are parameters associated with the patients: they are considered to be fixed and common for all GPs. γ_{kh} are parameters associated with the characteristics of the physicians. u_{kj} is an inter-physician random effect.

In intermediate steps of the model, the impacts of both the patient and physician characteristics were estimated separately. The results shown are extracted from the multi-level analysis, combining both patient and physician effects.

The period with data in the database for each GP varied from one to eight quarters, with 50 % of the GPs having data from less than five quarters. This could lead to statistical bias unless the sources of unequal probabilities of stay are fully controlled for in the covariates [49]. Previous research has shown that physicians' participation in surveys is mostly influenced by their workload, the organisation of their practice and their age [50, 51]. However, because these variables were already part of our econometric model, it was not necessary to modify the weight of GPs according to their length of stay in the database.

Finally, in a regression model, the statistical results must be interpreted in relation to a reference situation, which in this case was a young patient with the diagnosis "disorders of lipoprotein metabolism" (E78) when consulting a young male GP in a solo practice with a low workload.

3 Results

3.1 Patient Characteristics: Gender, Age and Medical Profile

Female patients were less likely to be prescribed patented statins compared to male patients (coefficient: −0.0972; $p = 0.0087$) (Table 4).

Furthermore, patient age had a major impact on the pattern of prescribing, with greater prescribing of patented statins among the youngest patients valid for medical profile 1 (dyslipidemia) and medical profile 3 (combination of profiles 1, 2 and/or 4). Patients aged 68–76 years with a medical profile 1 were prescribed fewer patented statins than patients aged 59–67 years with the same profile (coefficient: −0.252; $p = 0.0447$), while the latter patients were prescribed fewer patented statins than younger patients with profile 1 (58 years old and under) (coefficient: −0.191; $p = 0.0007$). Moreover, older patients (over 77 years old) with profile 3 were prescribed fewer patented statins than patients aged 59–67 years (coefficient: −0.422; $p \leq 0.0001$). The results for young patients with profile 1 as a reference situation are displayed in Table 4; Table 5 provides coefficients and probabilities for the comparisons among profiles and ages other than the chosen reference situation.

By contrast, the medical profile did not significantly affect the probability of prescribing a patented statin except for young patients with heart diseases (profile 2) who were prescribed a greater number of patented statins (coefficient: 0.3992; $p < 0.0007$) compared to young patients with dyslipidemia only (profile 1) (Table 4).

3.2 Physicians Characteristics

Older male physicians (over 57 years old) were more likely to prescribe patented statins (0.245; $p = 0.0417$) than younger male physicians (46 years old and under). For the eldest group of physicians, male physicians prescribe a greater number of patented statins than female physicians (coefficient: 0.283; $p = 0.018$) (Table 4).

Whether the medical practice was a solo or group practice also affected the prescribing of patented statins. GPs in group practices prescribed significantly fewer patented statins (coefficient: −0.178; $p = 0.0338$) compared with solo GPs. Moreover, the lowest physician workload

Table 4 Multilevel model of factors associated with prescribing patent-protected statins among GPs

Effect	Coefficient estimate	Standard error	Pr > |t| : statistical significance
Intercept	0.5634	0.3931	0.1527
Patient age and medical profile			
Age 1 (58 years and under)			
Profile 1 (dyslipidemia)	Ref	Ref	Ref
Profile 2 (heart disease)	0.3992	0.1178	*
Profile 3 (combination of profiles 1, 2 and 4)	−0.073	0.088	NS
Profile 4 (diabetes)	0.181	0.198	NS
Profile 5 (other)	−0.112	0.195	NS
Age 2 (59–67 years)			
Profile 1 (dyslipidemia)	−0.191	0.106	*
Profile 2 (heart disease)	−0.259	0.109	**
Profile 3 (combination of profiles 1, 2 and 4)	−0.167	0.084	**
Profile 4 (diabetes)	−0.198	0.210	NS
Profile 5 (other)	−0.021	0.216	NS
Age 3 (68–76 years)			
Profile 1 (dyslipidemia)	−0.442	0.118	**
Profile 2 (heart disease)	−0.417	0.103	**
Profile 3 (combination of profiles 1, 2 and 4)	−0.364	0.084	**
Profile 4 (diabetes)	−0.446	0.237	*
Profile 5 (other)	−0.535	0.207	*
Age 4 (over 76 years)			
Profile 1 (dyslipidemia)	−0.665	0.143	**
Profile 2 (heart disease)	−0.581	0.097	**
Profile 3 (combination of profiles 1, 2 and 4)	−0.589	0.084	**
Profile 4 (diabetes)	−0.131	0.315	NS
Profile 5 (other)	−0.281	0.202	NS
Patient gender			
Male	Ref	Ref	Ref
Female	−0.097	0.037	*
GP's activity sector			
Sector 1	Ref	Ref	Ref
Sector 2	0.026	0.188	NS
Physician age and gender			
Physician age 1 (46 years and under)-man	Ref	Ref	Ref
Physician age 1 (46 years and under)-woman	0.012	0.205	NS
Physician age 2 (47–51 years)-man	0.035	0.109	NS
Physician age 2 (47–51 years)-woman	−0.179	0.180	NS
Physician age 3 (52–57 years)-man	0.173	0.1172	NS
Physician age 3 (52–57 years)-woman	−0.068	0.2334	NS
Physician age 4 (over 57 years)-man	0.245	0.120	**
Physician age 4 (over 57 years)-woman	−0.789	0.412	*
Solo versus group practice			
GP solo	Ref	Ref	Ref
GP with hospital activity	−0.036	0.097	NS
GP in a group with other GPs	−0.178	0.084	**
GP in a group with one speciality + hospital	−0.015	0.134	NS
Physician workload			
1. 69 consultations/week and under	Ref	Ref	Ref
2. 70–88 consultations/week	−0.172	0.075	**
3. 89–111 consultations/week	−0.145	0.081	*
4. Over 111 consultations/week	−0.171	0.087	*

Note for the reader: *Ref* reference profile; *NS* not statistically significant; *statistically significant at a 10 % threshold; **statistically significant at a 5 % threshold

Fit statistics: −2 residual log pseudo-likelihood, 62878.86; generalised chi-square, 13887.40; generalised chi-square/DF, 0.97

The ratio of the generalised chi-square statistic and its degrees of freedom is below 1. This ratio is a measure of the residual variability in the marginal distribution of the data. It indicates that the variability in these data has been properly modelled and that there is no residual over dispersion

Source: Institute for Research and Information in Health Economics (IRDES). Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2009–2010

Table 5 Coefficients (C; first values) and significance tests (*p* value; second values) for the patient's age and medical profile variables

	A1P1	A1P2	A1P3	A1P4	A1P5	A2P1	A2P2	A2P3	A2P4	A2P5
A1P1		0.399	−0.07	0.181	−0.112	−0.191	−0.259	−0.167	−0.198	−0.021
		(0.0007)	(0.402)	(0.3601)	(0.5639)	(0.0711)	(0.0177)	(0.0468)	(0.345)	(0.9200)
A1P2	−0.399		−0.473	−0.218	−0.512	−0.59	−0.658	−0.566	−0.597	−0.42
	(0.0007)		(<0.0001)	(0.296)	(0.0128)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0067)	(0.0617)
A1P3	0.074	0.473		0.255	−0.039	−0.117	−0.186	−0.093	−0.125	0.052
	(0.402)	(<0.0001)		(0.189)	(0.839)	(0.233)	(0.067)	(0.201)	(0.546)	(0.806)
A1P4	−0.181	0.218	−0.255		−0.293	−0.372	−0.440	−0.348	−0.379	−0.203
	(0.3601)	(0.296)	(0.189)		(0.260)	(0.067)	(0.031)	(0.070)	(0.162)	(0.463)
A1P5	0.112	0.512	0.039	0.293		−0.078	−0.147	−0.054	−0.086	0.091
	(0.564)	(0.013)	(0.839)	(0.260)		(0.695)	(0.464)	(0.773)	(0.750)	(0.731)
A2P1	0.191	0.590	0.117	0.372	0.078		−0.068	0.024	−0.007	0.169
	(0.0711)	(<0.0001)	(0.233)	(0.067)	(0.695)		(0.5605)	(0.7991)	(0.973)	(0.442)
A2P2	0.259	0.658	0.186	0.440	0.147	0.068		0.092	0.061	0.238
	(0.0177)	(<0.0001)	(0.067)	(0.031)	(0.464)	(0.5605)		(0.3446)	(0.777)	(0.281)
A2P3	0.167	0.566	0.093	0.348	0.054	−0.024	−0.092		−0.031	0.145
	(0.0468)	(<0.0001)	(0.201)	(0.070)	(0.773)	(0.7991)	(0.3446)		(0.878)	(0.490)
A2P4	0.198	0.597	0.125	0.379	0.086	0.007	−0.061	0.031		0.177
	(0.346)	(0.007)	(0.546)	(0.162)	(0.750)	(0.973)	(0.777)	(0.878)		(0.534)
A2P5	0.022	0.421	−0.052	0.203	−0.091	−0.169	−0.238	−0.145	−0.177	
	(0.920)	(0.062)	(0.806)	(0.463)	(0.731)	(0.442)	(0.281)	(0.490)	(0.534)	
A3P1	0.442	0.842	0.369	0.623	0.330	0.252	0.183	0.276	0.244	0.421
	(0.0002)	(<0.0001)	(0.001)	(0.003)	(0.109)	(0.0447)	(0.1553)	(0.0106)	(0.269)	(0.062)
A3P2	0.417	0.816	0.343	0.598	0.305	0.226	0.158	0.250	0.219	0.395
	(<0.0001)	(<0.0001)	(0.001)	(0.003)	(0.123)	(0.0433)	(0.1624)	(0.0061)	(0.304)	(0.070)
A3P3	0.364	0.763	0.290	0.545	0.252	0.173	0.105	0.197	0.166	0.342
	(<0.0001)	(<0.0001)	(<0.0001)	(0.005)	(0.182)	(0.0644)	(0.2831)	(0.0034)	(0.417)	(0.103)
A3P4	0.446	0.845	0.372	0.627	0.333	0.255	0.186	0.279	0.247	0.424
	(0.0598)	(0.0006)	(0.111)	(0.032)	(0.252)	(0.2891)	(0.4399)	(0.2289)	(0.410)	(0.164)
A3P5	0.535	0.935	0.462	0.716	0.423	0.345	0.276	0.368	0.337	0.514
	(0.0096)	(<0.0001)	(0.023)	(0.008)	(0.098)	(0.1025)	(0.1930)	(0.0666)	(0.224)	(0.054)
A4P1	0.665	1.065	0.592	0.846	0.553	0.475	0.406	0.499	0.467	0.644
	(<0.0001)	(<0.0001)	(<0.0001)	(0.001)	(0.013)	(0.0015)	(0.0076)	(0.0002)	(0.047)	(0.007)
A4P2	0.581	0.981	0.508	0.762	0.469	0.391	0.322	0.415	0.383	0.560
	(<0.0001)	(<0.0001)	(<0.0001)	(0.001)	(0.016)	(0.0002)	(0.0027)	(<0.0001)	(0.068)	(0.009)
A4P3	0.589	0.988	0.515	0.770	0.476	0.398	0.329	0.422	0.390	0.567
	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.012)	(<0.0001)	(0.0008)	(<0.0001)	(0.056)	(0.007)

Table 5 continued

	A1P1	A1P2	A1P3	A1P4	A1P5	A2P1	A2P2	A2P3	A2P4	A2P5
A4P4	0.131	0.531	0.058	0.312	0.019	−0.059	−0.128	−0.035	−0.067	0.110
	(0.677)	(0.099)	(0.853)	(0.384)	(0.958)	(0.852)	(0.688)	(0.909)	(0.855)	(0.766)
A4P5	0.281	0.680	0.207	0.462	0.169	0.090	0.022	0.114	0.083	0.259
	(0.164)	(0.001)	(0.295)	(0.082)	(0.509)	(0.662)	(0.916)	(0.560)	(0.762)	(0.331)
	A3P1	A3P2	A3P3	A3P4	A3P5	A4P1	A4P2	A4P3	A4P4	A4P5
A1P1	−0.442	0.417	−0.364	−0.445	−0.535	−0.665	−0.581	−0.589	−0.131	−0.281
	(0.0002)	(<0.0001)	(<0.0001)	(0.0598)	(0.0096)	(<0.0001)	(<0.0001)	(<0.0001)	(0.6765)	(0.164)
A1P2	−0.841	−0.816	−0.763	−0.845	−0.934	−1.06	−0.98	−0.99	−0.531	−0.68
	(<0.0001)	(<0.0001)	(<0.0001)	(0.0006)	(<0.0001)	(<0.0001)	(<0.0001)	(<0.0001)	(0.0992)	(0.0014)
A1P3	−0.369	−0.343	−0.290	−0.372	−0.462	−0.592	−0.508	−0.515	−0.058	−0.207
	(0.001)	(0.001)	(<0.0001)	(0.111)	(0.023)	(<0.0001)	(<0.0001)	(<0.0001)	(0.853)	(0.295)
A1P4	−0.623	−0.598	−0.545	−0.627	−0.716	−0.846	−0.762	−0.770	−0.312	−0.462
	(0.003)	(0.003)	(0.005)	(0.032)	(0.008)	(0.001)	(0.001)	(<0.0001)	(0.384)	(0.082)
A1P5	−0.330	−0.305	−0.252	−0.333	−0.423	−0.553	−0.469	−0.476	−0.019	−0.169
	(0.109)	(0.123)	(0.182)	(0.252)	(0.098)	(0.013)	(0.016)	(0.012)	(0.958)	(0.509)
A2P1	−0.252	−0.226	−0.173	−0.255	−0.345	−0.475	−0.391	−0.398	0.059	−0.090
	(0.0447)	(0.0433)	(0.0644)	(0.2891)	(0.1025)	(0.0015)	(0.0002)	(<0.0001)	(0.852)	(0.662)
A2P2	−0.183	−0.158	−0.105	−0.186	−0.276	−0.406	−0.322	−0.329	0.128	−0.022
	(0.1553)	(0.1624)	(0.2831)	(0.4399)	(0.1930)	(0.0076)	(0.0027)	(0.0008)	(0.688)	(0.916)
A2P3	−0.276	−0.250	−0.197	−0.279	−0.368	−0.499	−0.415	−0.422	0.035	−0.114
	(0.0106)	(0.0061)	(0.0034)	(0.2289)	(0.0666)	(0.0002)	(<0.0001)	(<0.0001)	(0.909)	(0.560)
A2P4	−0.244	−0.219	−0.166	−0.247	−0.337	−0.467	−0.383	−0.390	0.067	−0.083
	(0.269)	(0.304)	(0.417)	(0.410)	(0.224)	(0.047)	(0.068)	(0.056)	(0.855)	(0.762)
A2P5	−0.421	−0.395	−0.342	−0.424	−0.514	−0.644	−0.560	−0.567	−0.110	−0.259
	(0.062)	(0.070)	(0.103)	(0.164)	(0.054)	(0.007)	(0.009)	(0.007)	(0.766)	(0.331)
A3P1		0.025	0.078	−0.003	−0.093	−0.223	−0.139	−0.146	0.311	0.161
		(0.8366)	(0.4640)	(0.9896)	(0.6684)	(0.1575)	(0.2374)	(0.1726)	(0.334)	(0.447)
A3P2	−0.025		0.053	−0.029	−0.118	−0.249	−0.164	−0.172	0.286	0.136
	(0.8366)		(0.5593)	(0.9043)	(0.5713)	(0.0924)	(0.1024)	(0.0597)	(0.367)	(0.506)
A3P3	−0.078	−0.053		−0.082	−0.171	−0.301	−0.217	−0.225	0.233	0.083
	(0.4640)	(0.5593)		(0.7245)	(0.3929)	(0.0247)	(0.0087)	(0.0008)	(0.454)	(0.672)
A3P4	0.003	0.029	0.082		−0.090	−0.220	−0.136	−0.143	0.314	0.165
	(0.9896)	(0.9043)	(0.7245)		(0.7636)	(0.3964)	(0.5648)	(0.5370)	(0.409)	(0.577)
A3P5	0.093	0.118	0.171	0.090		−0.130	−0.046	−0.053	0.404	0.254
	(0.6684)	(0.5713)	(0.3929)	(0.7636)		(0.5740)	(0.8228)	(0.7905)	(0.267)	(0.324)

Table 5 continued

	A3P1	A3P2	A3P3	A3P4	A3P5	A4P1	A4P2	A4P3	A4P4	A4P5
A4P1	0.223	0.249	0.301	0.220	0.130		0.084	0.077	0.534	0.384
	(0.1575)	(0.0924)	(0.0247)	(0.3964)	(0.5740)		(0.5555)	(0.5656)	(0.108)	(0.091)
A4P2	0.139	0.164	0.217	0.136	0.046	−0.084		−0.007	0.450	0.300
	(0.2374)	(0.1024)	(0.0087)	(0.5648)	(0.8228)	(0.5555)		(0.9305)	(0.152)	(0.135)
A4P3	0.146	0.172	0.225	0.143	0.053	−0.077	0.007		0.457	0.308
	(0.1726)	(0.0597)	(0.0008)	(0.5370)	(0.7905)	(0.5656)	(0.9305)		(0.141)	(0.116)
A4P4	−0.311	−0.286	−0.233	−0.314	−0.404	−0.534	−0.450	−0.457		−0.150
	(0.334)	(0.367)	(0.454)	(0.409)	(0.267)	(0.108)	(0.152)	(0.141)		(0.679)
A4P5	−0.161	−0.136	−0.083	−0.165	−0.254	−0.384	−0.300	−0.308	0.150	
	(0.447)	(0.506)	(0.672)	(0.577)	(0.324)	(0.091)	0.135)	0.116)	(0.679)	

Note for the reader the probability that a patient A2P2 [a patient whose age is 2 (59–67 years old) and profile 2 (heart disease)] is being prescribed patented statins is not significantly different from the probability that a patient A2P3 [a patient whose age is 2 (59–67 years old) and profile 3 (complex profile)] is being prescribed patented statins

Conversely, the probability between A2P2 and A1P2 is significantly different

Source: Institute for Research and Information in Health Economics (IRDES)

Data: IMS-Health Permanent Survey on Medical prescription (EPPM) 2009–2010

was associated with greater prescribing of patented statins (Table 4). The GP sector had no impact on the probability of prescribing patented statins (for GPs in sector 1, fees are fixed by the national public Health Insurance, whereas GPs in sector 2 are allowed to charge higher fees).

4 Discussion

This study has shown that there is considerable variation among physician types with respect to their prescribing habits, which reflects similar results to those obtained in other studies [33]. Consequently, there is a need to maximise the impact of educational activities to counteract the influence of pharmaceutical companies [52–59] when resources for outreach visits are scarce.

4.1 Comparison with Existing Literature

Regarding patient characteristics, age had a positive effect on the prescribing of multiple-sourced statins for two medical profiles both the simplest and the most complicated. The effect of the patient's age might be explained by a greater fear among prescribers regarding adverse effects from the more recently registered drugs rosuvastatin or atorvastatin. It is well documented that uptake of new drugs varies between different prescribers [60], suggesting that prescribers apply different prescribing strategies for old and young patients. In addition, physicians may be unwilling to switch treatment among older patients who have been prescribed statins for a long time, and these statins are now available as generics.

We believe that the increased prescribing of patented statins, namely, atorvastatin or rosuvastatin, in the presence of heart disease in younger patients could be explained by the higher LDL cholesterol reduction that is achieved with rosuvastatin and atorvastatin compared with other statins [61], which has been endorsed by the French National Authority of Health (HAS) in their guidelines [35]. On the physician side, older age, solo practice and low activity had a positive impact on the prescription of patented statins. This impact was greater for male than for female physicians. For male physicians, the effect of age is consistent with previous studies [38], which have shown that physicians who have more recently received their medical education are more likely to adopt best practices. However, we found an opposite effect for older female physicians, who tended to prescribe more multiple-sourced statins. This result underlines the importance of carrying out separate studies for both male and female physicians in France, as well as when directing educational resources and other interventions.

The influence of lower physician workload on the prescribing of patented statins is more difficult to interpret. On

the one hand, these physicians have more time to see pharmaceutical company representatives than their busier counterparts. Conversely, physicians with low activity are not the main target group for pharmaceutical representatives. However, as discussed, previous research has demonstrated the influence of pharmaceutical company marketing activities, including promotional items, in changing prescribing behaviour, especially as companies have been seen as an important source of prescribing information in the past [52–59]. As a result, some countries and regions now restrict pharmaceutical company activities and include potential fines for abuse [8, 62]. However, in France, such activities will be more difficult to implement, with 78 % of GPs seeing more than 10 pharmaceutical company representatives monthly [63]. In addition, previous studies demonstrated that French physicians see a greater number of pharmaceutical company representatives than their European counterparts, with one medical sales representative for every nine physicians [64]. This ratio compares with the Netherlands where there was only one medical sales representative per 34 physicians [64]. Despite regulations regarding pharmaceutical company activities in their quality and quantity of information [64], spending on marketing activities in France is still considerable and was estimated at 3.28 billion euros in 2010, if marketing activities represent at least 12 % of total company turnover.

Some studies have shown that group practices are associated with a higher quality of care compared to solo practices [41], but most studies have focussed on preventive care. We found only one study assessing the impact of the organisational structure on drug prescriptions, but this study showed no substantial differences for the two quality indicators related to the medication management of chronic diseases [42]. Consequently, further research is needed to substantiate our results showing that group practices and participation in hospital activities are associated with greater prescribing of multiple-sourced statins.

4.2 Implications for Policy and Practice

This study shows that French physicians still prescribe an appreciable and increasing proportion of patented statins (60 % of all statin prescriptions in 2011) at the expense of equally effective and cheaper multiple-sourced statins. This result is contrary to other European countries that have instigated multiple demand-side measures to improve prescribing efficiency [4].

Greater prescribing of multiple-sourced statins could be achieved by building on the demand-side measures outlined in Box 1 [1, 4, 5, 27]. Educational outreach visits conducted by Health Insurance Medical Representatives and Practitioners have been in existence since 2004. We believe that the value of our study is that the efficiency of educational outreach visits could be enhanced if visits were focused initially on those physicians who are likely to prescribe a greater proportion of patented statins, i.e., solo GPs, older GPs and GPs with a lower workload.

Combined with greater targeting of academic detailing activities and other demand-side measures, the P4P pilot programme that was extended to all GPs in 2011 should enhance statin prescribing efficiency in the future [29]. If the ambitious target for statins (70 % of all prescriptions being multiple-sourced statins) in the P4P programme had been achieved throughout France, savings for health insurance would have been at least €166 million per annum.

Additional initiatives could include an increase in out-of-pocket expenses for patients receiving patented statins or the introduction of prior authorization policies. Such policies cannot currently be applied in France since patient copayments are currently based on the severity of the disease and the efficacy of the drug and not according to generic versus originator or patent products in the class and prior authorisation schemes cannot be applied (article R163.3 of the French Social Security Code). However, they could lead to a substantial decrease in the number of patent-protected statin prescriptions [65, 66].

4.3 Strengths and Limitations

There are limitations to our study. In our final sample, 81 % of physicians were men and 19 % women, while before filtering on a minimal level of statin prescriptions, 73 % of physicians were men and 27 % were women. The sample reduction leads to other statistical differences. In the final sample, the GPs are slightly older, work more often in monodisciplinary group practices and have a higher workload. All differences in the physician variables are statistically significant. Conversely, the sample reduction had no consequences at the patient level because the characteristics of patients do not significantly change before and after filtering on a minimal level of statin prescriptions.

Consequences at the physician level are easily explained by the design of the survey, which is collected for each GP and contains information on all of his/her patient visits over a 7-day period. Thus, the selection of physicians with at least 20 statin prescriptions restricts the sample to older physicians who are more frequently male and have a higher workload. We are aware that this sample is skewed towards male physicians with 73 % of physicians in the initial sample being men and 27 % women. However, these were the characteristics of the physicians who prescribed multiple-sourced statins, in line with our inclusion criteria. Furthermore, this sample reduction proved to have no

impact on the results. We tested the multilevel model on samples with at least 15 or 10 statin prescriptions per GP and did not observe any significant changes in the results (electronic supplementary material Tables 1 and 2).

Limitations of our study include the reliability of the "patient's medical profile", because this profile is based on the diagnoses completed by the physician during the consultation. It is likely that participating physicians may not always provide a complete report of the diseases. Moreover, the database used in this study does not allow for tracking the patient over time; consequently, it was not possible to disentangle initial treatments from repeated prescriptions. Furthermore, the database contains limited information to help understand the appropriateness of the prescriptions. For instance, there is no information on LDL cholesterol levels in the patient's medical records. If this information had been available, it might have been possible to determine the rate of rational prescribing and therefore the extent of potential savings from improved prescribing of generic statins. The frequency of visits from pharmaceutical representatives to physicians' offices and the extent of continuous medical education including visits from health insurance institutions are also unknown. In addition, the quality of the collected information depends on the accuracy of the GPs in completing the survey. However despite these limitations, we suggest that profiling physicians is valuable to both health authorities and researchers in order to evaluate the impact of any future demand-side measures, such as academic detailing (educational outreach visits) and their pedagogic design.

5 Conclusion

Overall, there is a need in France to combine and reinforce several aspects of demand-side initiatives in order to improve both the quality and the efficiency of prescribing drugs. This study shows that statin prescriptions are quite heterogeneous among GPs, with age, group practice and physician workload being factors that influence the prescribing of patented statins. Consequently, demand-side measures, such as academic detailing, need to be targeted to maximise their effectiveness in the absence of sufficient resources available for their implementation. This conclusion resonates with previous research that advocates for multiple interventions to improve the quality and efficiency of prescribing [4, 5, 18, 20, 67, 68]. In the first instance, activities such as improved targeting of educational outreach visits can be aimed at drug classes where both multiple-sourced and patented products exist and are seen as essentially similar in all or nearly all patients. In France, as in other countries, it could be wise to invest in prescriber and expert driven resources for strengthening work with drug recommendations and follow-up of prescribing through Drug and Therapeutics Committees and clinical pharmacological services [69]. Therefore, increasing the prescribing of generic drugs without compromising care would enable considerable savings.

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