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RESEARCH ARTICLE



## Generic dispensing rates for substitutable drugs prescribed by general practitioners compared with other private ambulatory specialists: A study based on a French national reimbursement database

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### KEY MESSAGES

- 82% of substitutable drugs prescribed by French private general practitioners in 2019 were dispensed in generic form.
- No other ambulatory specialty rated significantly higher than general practitioners.
- Research is needed to study reasons for non-generic drug prescription in the context of legislative changes.

### ABSTRACT

**Background:** The use of generic drugs is a way for healthcare systems to reduce costs, particularly in ambulatory care. Several studies suggest that the prescriber's speciality is associated with the use of generic drugs, and that substitutable drugs prescribed by General Practitioners (GPs) are more often generic, but this association has never been studied in France. In the French legislative context, except in rare situations, all substitutable drugs prescribed should be dispensed in generic form.

**Objectives:** Compare the generic drugs dispensing rate among substitutable drugs dispensed in community pharmacies prescribed by French private GPs with that of other private specialists, all other specialities combined (first objective) or each other speciality taken individually (second objective).

**Methods:** We used a sample of an open available semi-aggregated database from the 2019 French health insurance system database. We compared with logistic regression models GPs to all other specialities combined, then GPs to the 19 other specialties taken individually, only on the substitutable drugs they prescribe in common.

**Results:** In 2019, 53.4% of the drugs prescribed by French private ambulatory physicians were substitutable drugs, and 81.5% of them were dispensed in generic form. After adjustment, the generic dispensing rate for substitutable drugs was significantly higher for GPs than for other specialties (ORa 0.74 [IC95% 0.72–0.76]). Thirteen of the nineteen other specialties taken individually, such as endocrinologists (ORa 0.64 [IC95% 0.57–0.72]) and cardiologists (ORa 0.60 [0.56–0.63]) had significantly lower generic dispensing rates than GPs. No other speciality had a rate significantly higher than GPs.

**Conclusions:** Substitutable drugs prescribed by French private GPs are more often dispensed in generic form than those from other private ambulatory specialties. To understand this result and optimise the use of generic drugs in outpatient settings, we need to study the different stages of drug use, from prescription by the physician to dispensing by the pharmacist and acceptance by the patient.

### ARTICLE HISTORY

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Drugs; generic; pharmacoepidemiology; database; primary health care; general practice

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## Introduction

For several decades, World Health Organisation (WHO) has been recommending the deployment of policies to promote the development of and access to generic drugs [1]. Most of drugs on the WHO essential medicines list are off patent and available as generics [2]. They are offered at lower prices than brand name drugs, thus reducing costs for patients and the health system, particularly in primary care [3]. In this framework the European Union pharmaceutical policy aims to optimise drugs use and rationalise the cost of pharmaceuticals [4].

Market share of generic drugs differs across countries [5]. According to the data from the Organisation for Economic Cooperation and Development (OECD) in 2018, among the 14 countries surveyed, Switzerland, Italy and France were the countries with the lowest volume shares of generic drugs in the total pharmaceutical market with 20.8%, 26.8% and 29.9%, respectively. In contrast, Canada, Slovakia, and the Czech Republic had the highest market shares by volume with 76.0%, 64.5% and 63.3%, respectively [6]. Some of these variations can be explained by specificities of national markets related to regulatory structures and health systems, including differences in policies related to prescribing, substitution, reimbursement conditions and drug pricing [3].

Worldwide, studies conducted in countries with different generic drug policies, and few in France, have investigated factors associated with generic drugs use and have been combined in reviews [7–12]. Some of these studies suggested that generic drugs use were different across prescriber specialties [11,13,14]. For example, Federman et al. found in the United States in 2007 that patients over 66 with heart disease followed by a cardiologist were less likely to use generic drugs than those followed by a General Practitioner (GP) only [14].

French National Health Insurance provides a high level of reimbursement for drugs, from 15% to 65% and up to 100% for chronic diseases, which are classified as ‘long-term conditions’. In France since 1999, pharmacists can substitute drugs under some conditions, i.e. dispensing a generic drug instead of prescribed brand name [15]. Drugs that can be substituted are listed in the generic drug list, which includes brand name drug and associated generic drugs [16]. Consumers can oppose substitution but must advance payment before reimbursement. Since 2015, French physicians are obliged to include on the prescription the International Non-proprietary Name (INN) alone or in combination with a brand name or specific generic

drug name [17]. In France, as of 2019, a pharmacist may provide a generic drug in place of the prescribed brand name drug if the prescribed drug is on the generic drug list, there is no specific prohibition against substitution mentioned on the prescription, and the patient does not object to the substitution. Thus, in the French legislative context, except in rare situations, all substitutable drugs prescribed should be dispensed in generic form, regardless of the prescriber’s specialty.

To our knowledge, there were no studies conducted in French setting using an exhaustive national database and focused on prescriber specialities in ambulatory care sector.

Our objectives were to compare the generic drugs dispensing rate among substitutable drugs dispensed in community pharmacies prescribed by private GPs with that of other private specialists, all other specialties combined (first objective) or each other speciality taken individually (second objective).

## Methods

### Data source

This study was a cross-sectional analytical study using data from Open Medic, an open access claims database produced by the French National Health Insurance [18]. Open Medic data are semi-aggregated database from the National Health Data System (SNDS) available in open access [19]. It includes all reimbursed drugs dispensed in community pharmacies. This study concerns data for 2019. Drugs are identified using the anatomical therapeutic chemical (ATC) classification [20] and a 13-digit drug package identification number used in France (Code CIP) [21]. Reimbursement data and number of individual packages dispensed during the year are presented according to descriptive elements on beneficiaries (age group, gender, province of residence) and prescriber’s specialty, resulting in a ‘drug-beneficiary-prescriber’ profile.

### Ethical aspects

This retrospective study, using a public database available on an open access basis which does not include human subjects, was conducted in accordance with the guidelines for Scientific, Technical and Medical (STM) journals [22]. The producer of the database (Caisse nationale de l’assurance maladie) performed data processing in order to guarantee the confidentiality of information on beneficiaries and healthcare professionals. The ethics committee of the CNGE (Collège

Nationale des Généralistes Enseignants) (n°IRB IRB00010804) has issued an opinion on this study (n° 140324583) and confirms that the study was conducted in accordance with the regulations.

### **Selection criteria**

#### **Drug selection**

This study was restricted to drugs belonging to the French generic drug list in 2019 i.e. substitutable drugs. For example, brand name drug containing semaglutide 1 mg is not a substitutable drug because it is protected by a patent, so there are no generic forms of semaglutide 1 mg on the French market. Conversely, brand name drug containing ramipril 1.25 mg is no longer protected by a patent and is therefore a substitutable drug, and there are generic forms of ramipril 1.25 mg on the French market. A generic group is defined by an active substance (or combination), a dosage and a pharmaceutical form. Each group includes the brand name drug with the associated generic drugs. For example, '[brand name] 10 mg/160 mg, amlodipine 10 mg+valsartan 160 mg, film-coated tablet'

Drugs whose prescription was restricted to specific prescribers were excluded to allow comparability between prescribers ([Appendix 1, supplementary material](#)).

There may have been situations where the reference drug or all the generic drugs in a group were not available in 2019. This may occur in the event of a stock shortage or when a generic group was created before the group's generics are marketed. To avoid bias, we have only included drugs from generic groups for which at least one reference drug and at least one generic drug from the group were dispensed in 2019.

#### **Selection of 'drug-beneficiary-prescriber' profiles**

This claims database contains negative drug consumption data corresponding to claims wrongly reimbursed in the previous year. This situation is exceptional, and we have decided to exclude them because it did not correspond to consumption data for the year analysed. Few profiles with missing data, corresponding to intentional missing data to ensure confidentiality when a total of 10 beneficiaries was not met, were also excluded.

Then profiles for which the prescriber's speciality was not known (salaried prescribers, mainly hospital physicians) and non-physician prescribers (i.e. midwives, dentists, etc.) were excluded. Salaried ambulatory physicians were therefore not included in the

analysis. In the French healthcare system, most ambulatory physicians are 'private'. However, this does not mean that consultations are not covered by the national health insurance system. Private practice differs from salaried practice in that physicians are paid on a fee-for-service model. The cost of consultations is set by the health insurance system. Patients are reimbursed the same amount whether they consult a private or salaried ambulatory physician, with the exception of physicians who charge extra fees.

### **Sampling**

#### **Analysis sample**

Given the computational time needed for analysing the whole database, after application of the selection criteria we performed a 1:1000 random sampling of profiles. Each profile had a probability of being randomly selected equal to its number of individual packages (generic or brand name) over the total number of individual packages in the database. Replacement was possible. Thus, in the analysis sample, each line corresponded to a single individual package of drug associated with a 'drug-beneficiary-prescriber' profile.

#### **Sub-samples**

The analysis sample contained drugs that had not been prescribed by each speciality. To compare GPs with each of the other specialities individually, 19 sub-samples were created. Each of these sub-samples only included drugs belonging to the generic groups in common between the two specialities studied. In these sub-samples, GPs were compared with other specialists only for the substitutable drugs they prescribed in common.

### **Outcome, explanatory variable, and confounding factors**

#### **Outcome**

The outcome was the generic drugs dispensing rate among substitutable drugs dispensed in community pharmacies. For each individual package dispensed an Open Medic variable (TOP\_GEN) identified if the individual package was a brand name drug or a generic drug. Thus, percentages of individual packages of generic drugs dispensed over the total number of drugs dispensed were calculated for each prescriber speciality. It was checked and corrected, where necessary, using the public medicines database of the French National Agency for the Safety of Medicines and Health Products [23].

### Explanatory variables

The explanatory variable was the physicians' specialties. An Open Medic variable (PSP\_SPE) identified the private prescriber's specialty in 22 categories. Three specialties, with very few prescriptions (radiologists, anatomopathologists and laboratory physicians), were grouped together as 'non-clinical specialties'. For the first objective, the explanatory variable was a binary variable: GPs versus the 21 other specialties combined. For the second objective, the explanatory variable was also binary: GPs versus each of the other specialties taken individually.

### Potential confounders

Three beneficiary-related characteristics known to be associated with generic drugs use and available in Open Medic were selected as potential confounders: age groups (strictly under 20, between 20 and 60 and strictly over 60), gender (female or male) and province of residence (13 categories) [11].

A variable identifying drug with a narrow therapeutic index was created and selected as a potential confounding factor because these drugs may be associated with different prescribing and dispensing behaviour from other drugs, and their use may differ between specialties. The list of drugs with a narrow therapeutic index was defined based on the list of active

**Table 1.** Generic dispensing rate for substitutable drugs according to the characteristics of drugs in the analysis sample.

	Total (%)	Dispensing generic drugs rate (%)
	<i>n</i> = 870,338	81.5
Anatomical therapeutic chemical classification 1		
Alimentary tract and metabolism	20.4	85.9
Blood and blood forming organs	1.5	84.5
Cardiovascular system	20.5	82.1
Dermatologicals	4.4	84.3
Genito-urinary system and sex hormones	2.9	78.9
Systemic hormonal preparations, excluding sex hormones and insulins	4.8	45.7
Antiinfectives for systemic use	9.1	95.5
Antineoplastic and immunomodulating agents	0.2	50.7
Musculo-skeletal system	6.1	88.1
Nervous system	23.1	78.4
Antiparasitic products, insecticides and repellents	0.1	55.5
Respiratory system	4.9	86.1
Sensory organs	2.0	54.9
Various	0.1	71.5
Drugs with a narrow therapeutic index or requiring special precautions <sup>a</sup>		
True	4.7	22.9

For each variable, the first column represents the percentage of the total variable (column %) and the second column represents the percentage of the variable's category (row %).

<sup>a</sup>List of the molecules concerned from the French authorities and the generic drug list product by the French Medicines Agency.

ingredients identified in French legislation (Appendix 2, supplementary material) [24].

### Statistical analysis

Descriptive data for the drugs, and prescribers in the analysis sample are described in Tables 1 and 2. The categorical variables are reported as a percentage of the total number of individual packages of drug dispensed. The generic drugs dispensing rate among substitutable was calculated as the total number of individual packages of generic drugs dispensed divided by the total number of individual packages dispensed for substitutable drugs (i.e. the brand name drug and its associated generic drugs).

The association between generic drugs dispensing rate and physicians' specialties was studied using logistic regression models adjusted for beneficiary and drug characteristic. Adjusted Odds Ratios (aOR) and their 95% confidence intervals were calculated, and Wald tests were performed. A  $p < 0.05$  was considered statistically significant.

Statistical analyses were performed using R (v4.2.2).

### Results

A flow diagram (Figure 1) shows the various stages involved in creating the analysis sample for the first

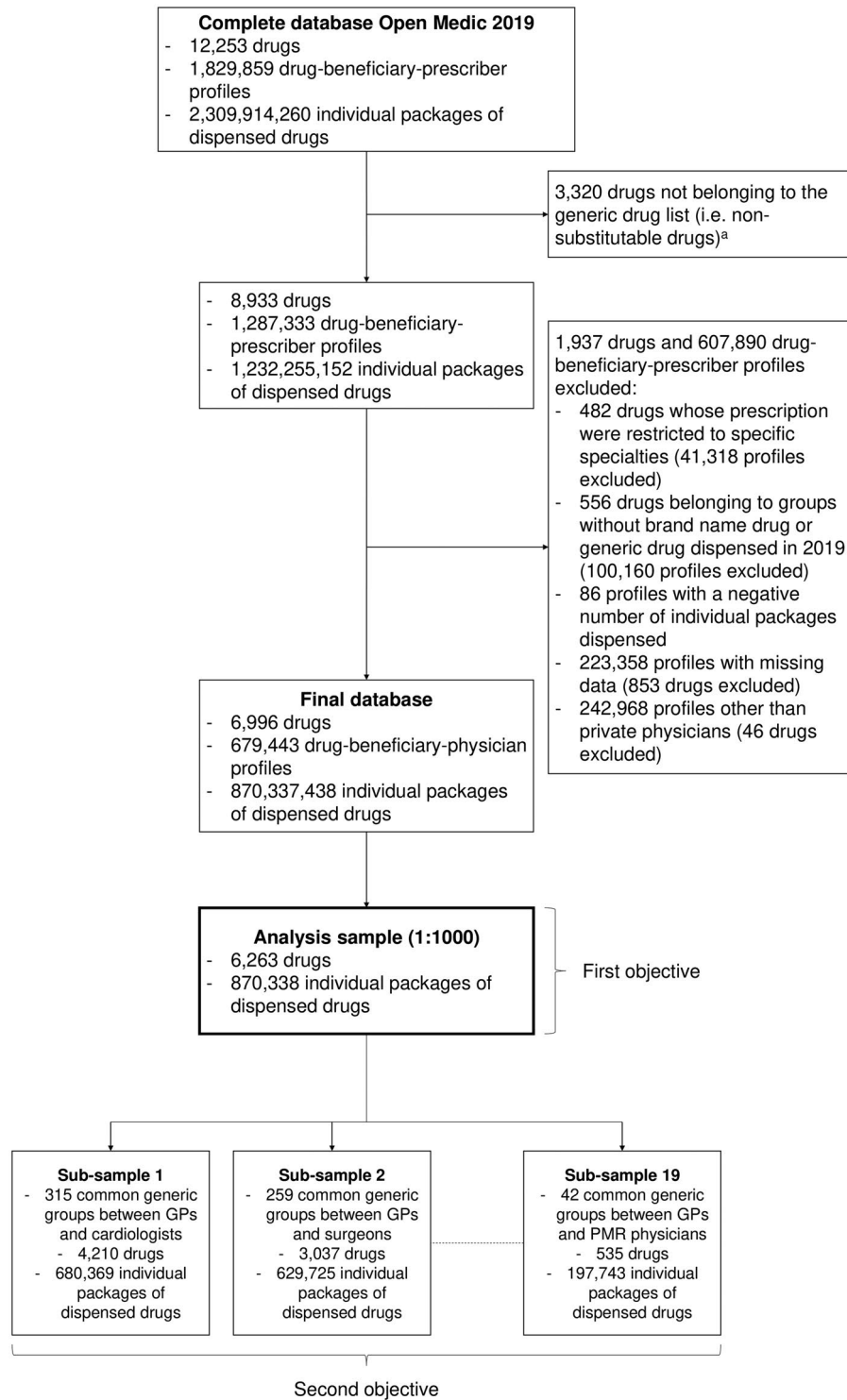
**Table 2.** Generic dispensing rate for substitutable drugs according to the prescriber's speciality in the analysis sample.

	Total (%)	Dispensing generic drugs rate (%)
	<i>n</i> = 870,338	81.5
Physicians' specialties		
General Practitioners	88.9	82.2
Other specialties	11.1	75.7
Other specialties (detail)		
Anesthesiologists	0.6	67.5
Cardiologists	9.1	75.9
Dermatologists	7.5	80.2
Endocrinologists	4.1	60.4
Gastroenterologists	3.1	80.2
Gynaecologists	8.9	81.0
Internists	1.6	70.7
Nephrologists	1.9	86.3
Neurologists	3.2	53.0
Non-clinical specialties	1.9	74.0
Ophthalmologists	10.6	48.5
Otolaryngologists	3.8	85.8
Paediatricians	7.2	87.1
Psychiatrists	19.6	81.6
PMR Physicians	0.2	83.9
Pulmonologists	2.5	80.6
Rheumatologists	5.7	80.2
Stomatologists	1.1	94.1
Surgeons	7.4	78.3

For each variable, the first column represents the percentage of the total variable (column %) and the second column represents the percentage of the variable's category (row %). PMR: Physical Medicine and Rehabilitation physicians.

objective and the nineteen sub-samples for the second objective. 46.5% of individual packages dispensed were excluded because they were not included in the generic drug list (i.e. non-substitutable drugs). GPs prescribed more substitutable drugs than the other specialties combined, with 54.3% and 49.5%, respectively.

Details of the percentage of individual packages of substitutable drugs prescribed by speciality are available in [Appendix 3, supplementary material](#). Application of the other drugs and profiles selection criteria obtained a final database of 679,443 profiles including 6,996 drugs and 870,337,438 individual packages of



**Figure 1.** Flow chart from initial database to the analysis sample and Sub-samples. <sup>a</sup>From 12/26/2019 version of the generic drug list produced by the French Medicines Agency. ATC: Anatomical Therapeutic Chemical. GPs: General practitioners. PMR: Physical Medicine and Rehabilitation physicians.

dispensed drugs. The number of profiles with missing data represented 1.1% of all individual packages dispensed. [Appendices 4 and 5, supplementary material](#), provide a visual comparison between the analysis sample and the final database.

Characteristics of the analysis sample are presented in [Tables 1 and 2](#). Using ATC1 classification, the most dispensed drugs classes were 'Nervous system', 'Cardiovascular system' and 'Alimentary tract and metabolism' with 23.1%, 20.5% and 20.4% of the individual packages dispensed, respectively ([Table 1](#)). For one individual package dispensed as a brand name, 4.4 were dispensed as generics. The generic drugs dispensing rate by ATC1 classification ranged from 95.5% for 'Antiinfectives for systemic use' to 45.7% for 'Systemic hormonal preparations, excluding sex hormones and insulins'. Individual packages identified by the 'Drugs with a narrow therapeutic index or requiring special precautions' variable were mostly dispensed as brand names (77.1%) ([Table 1](#)). In the analysis sample, 58.8% of individual packages of substitutable drugs were dispensed to beneficiaries aged over 60, 35.1% to those aged between 20 and 59 and 6.1% to those aged under 20. As the age category decreases, the generic dispensing rate increases, from 80.8% to 81.4% and 87.3%, respectively. Moreover, 57.8% of individual packages of substitutable drugs were dispensed to women, with a generic dispensing rate of 80.4% compared with 82.9% for men. GPs prescribed 88.9% of individual packages of substitutable drugs dispensed. Psychiatrists, ophthalmologists, and cardiologists were the other most represented specialties with respectively 2.2%, 1.2% and 1.0% of prescriptions of individual packages dispensed.

The generic drug-dispensing rate for individual packages prescribed by GPs was 82.2% [IC95% 82.1–82.3], versus 75.7% [IC95% 75.4–76.0] for those prescribed by the other specialties combined ([Table 2](#)). After adjustment, the generic drug-dispensing rate for individual packages prescribed by GPs was significantly higher than that for the other specialties combined, with an aOR of 0.74 [CI95 0.72–0.76] ( $p < 0.01$ ).

[Figure 2](#) shows the results for the second objective, and [Appendix 6, supplementary material](#), shows the generic groups shared by GPs and other specialists, which were used to establish the sub-samples. For the second objective, there were no other specialties with aOR significantly greater than 1 ([Figure 2](#)). Thus, no other specialty had a generic drug-dispensing rate for individual packages significantly higher than that of GPs. Anaesthetists, gynaecologists, nephrologists, Physical Medicine, and Rehabilitation (PMR) physicians, stomatologists and surgeons did not have an aOR

significantly different from 1. Cardiologists, dermatologists, endocrinologists, gastroenterologists, internists, neurologists, non-clinical specialists, ophthalmologists, otorhinolaryngologists, paediatricians, psychiatrists, pulmonologists, and rheumatologists had aOR significantly less than 1. Neurologists and paediatricians had the lowest aOR at 0.44 [IC95% 0.39–0.49] and 0.53 [IC95% 0.48–0.58], respectively.

## Discussion

### Main findings

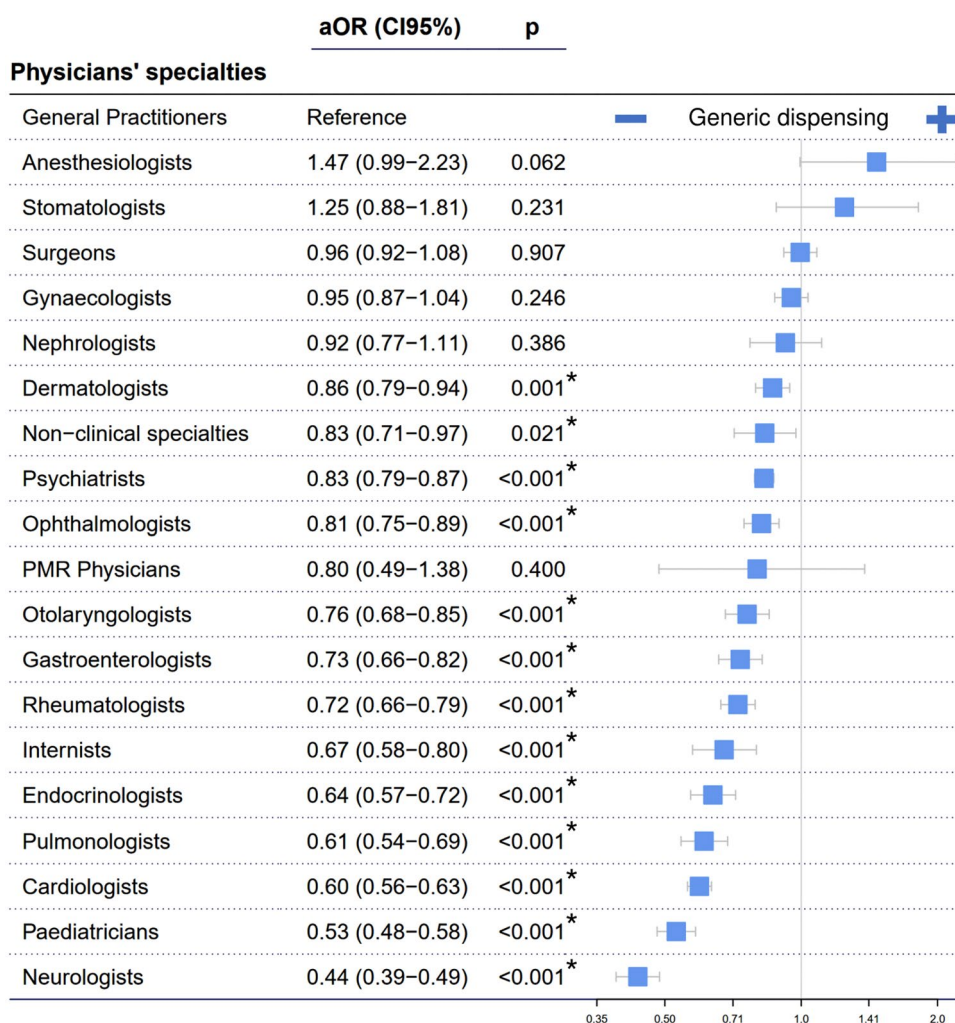
This study found a significant difference between the generic drug-dispensing rate among substitutable drugs dispensed in community pharmacies and the prescribing physician's specialty among French private practitioners based on a French national drug-dispensing database in 2019. When focusing on the comparison between each specialty individually and GPs restricted to drugs belonging to same generic groups, those prescribed by GPs were more often dispensed as generics than other specialties except for anaesthetists, gynaecologists, nephrologists, PRM physicians, stomatologists, and surgeons for which no significant associations were found.

### Strengths

This study was based on the French insurance system database, which provided access to all French annual data for drugs dispensed in community pharmacies. Dispensing represents the last stage of drug use before consumption by patients and no differential consumption between generic and brand name drugs are expected after dispensing [25,26]. All physicians' specialties were studied, and, to our knowledge, this had not been done previously. One of us (Hugo Figoni) manually checked data in Open Medic to limit potential classification bias and several potential confounding factors were considered in the analysis, particularly drug-related variables. Finally, this study was, to our knowledge, the first to focus on the French setting using exhaustive community dispensing data.

### Limitation

Our study has some limits. First, there was no information in Open Medic on prescription details or longitudinal data. Thus, it was not possible to have information on the presence of 'Not for Generic Substitution' (NGS) mention, the number of drugs prescribed or to reconstruct therapeutic sequences. It was not possible to



**Figure 2.** Forest Plot showing the association between the generic drug-dispensing rate among substitutable drugs and the specialty of the prescribing physicians in a 2 by 2 comparison with GPs as reference in Sub-samples including only drugs in common. An aOR under 1 indicates that substitutable drugs prescribed by specialist physicians are less often dispensed as generics than those prescribed by GPs. Confidence intervals are represented by vertical lines around the boxes. A vertical line not intersecting the vertical bar indicates a statistical difference from the reference. Adjustment variables: age groups of beneficiaries (strictly under 20, between 20 and 60 and strictly over 60), gender of beneficiaries (female or male) and province of residence of beneficiaries (13 categories), and the generic groups defined by the French Medicines Agency. Test used in logistic regression models: Wald test. Non-clinical specialties: laboratory physicians and radiologists. aOR: Adjusted Odd Ratio. PMR: Physical Medicine and Rehabilitation physicians. An asterisk (\*) indicates a statistical difference from the reference (general practitioners)

study substitution as it was unknown whether a branded or generic drug was prescribed.

Information on physicians' socio-demographics, which is related to generic drugs use are not available in Open Medic [27]. A systemic review with meta-analysis conducted in 2018 by Mishuk et al. showed that patients with lower income used more generic drugs [28]. In our study, it was not possible to include beneficiaries' socio-economic data. There was also no information on community pharmacies, although the type (individual/chain) or the emplacement (rural/urban) of pharmacies were known to be associated with generic drug use [29–31]. Thus, some potential confounding factors may

not have been measured and included in the multivariate analysis, and their absence may have biased results in both directions.

### Literature comparison

To interpret dispensing data, it is necessary to retrace the drug use chain from prescription to dispensing, considering three main protagonists: physicians, community pharmacists, and patients.

A 2009 study in the US context found no association between physician specialty and their perceptions of generic drugs [27]. It would be interesting to

conduct more studies, both quantitative and qualitative, investigating perceptions between medical specialties in other settings.

French GPs who did not receive gifts by the pharmaceutical industry were prescribed significantly more generic antibiotics, antihypertensives and statins than those who did [32]. Similar results were also found in other countries [13,33]. The influence of industry payment was quite consistent across the different specialties [13]. Thus, there are perhaps differences in the relationship between physicians and industry across specialties in France that may explain some of our results.

Prescribing behaviours are acquired in part during training and have been shown to remain stable during practice [34]. Brand-name prescribing of young residents was influenced by the prescribing of their mentors [35]. The residency in general practice takes place partly in an ambulatory setting in contrast to the residency in other clinical specialties which take place only in a hospital. Thus, the differences observed in our study between specialties could be related to physicians' training.

Our results are consistent with those of Qian et al. who, in the US context in 2013, showed that there were higher generic drugs prescribing rate among primary care physicians compared to physicians in other medical and surgical specialties [13]. In 2007, Federman et al. found that US patients over 66 years old followed by a cardiologist were less likely to use generic drugs than those followed by a GP only (75% vs. 81%) [14]. We found similar results.

Another study suggests that physician could influence generic drugs dispensing by pharmacist [11]. However, fewer studies were conducted on pharmacists and no studies evaluating the impact of prescriber specialty on pharmacists' generic drugs dispensing were found.

A review of patient perception, has shown that the perception of generic drugs, across the world, has improved over time [9]. The influence of healthcare professionals on consumers' acceptance of generic drugs was significant despite their lack of trust [9,12]. However, this influence according to the prescriber's specialty has not been studied, and this may be a clue to explain the results of our study. The specificities of the care relationship and communication between GPs and their patients may provide a clue to explain some of our results.

In our study, almost half of the individual packages dispensed did not belong to the generic drug list, which is consistent with the literature [6]. Patent drugs prescribing limits substitution and generic drugs use. This

partially explains why France is one of the high-income countries with the lowest use of generic drugs.

The least substituted drugs, in our study, were those in 'Systemic hormonal preparations, excluding sex hormones and insulins' ATC class. This result is consistent with Segal et al. [30] where thyroid hormones were the least substituted drugs, and Beauvais et al. where the term NGS is most commonly used [36].

In France in 2020, a new law limited the use of NGS mentioned by physicians to specific situations: prescribing drugs with a narrow therapeutic index, prescribing drugs to children under 6 years of age when no generic drug has a suitable galenic form, prescribing drug for a patient with a formal and proven contraindication to an excipient with a known effect [24]. These legislative changes may have led to changes in prescribing behaviour since 2019 it would be interesting to study.

Further studies could be conducted to improve understanding of the relationship between prescriber specialty and generic drugs dispensing rate to further optimise generic drugs use and thus rationalise healthcare spending.

Studies have shown that private physicians used NGS mention more often than salaried physicians, and that physicians in exclusive private practice had a worse perception of generic drugs than salaried physicians [37]. It might be interesting to conduct a similar study comparing private physicians with salaried physicians in ambulatory care.

## Conclusion

Substitutable drugs prescribed by French private GPs are more often dispensed in generic form than those from other ambulatory specialties. This remains true for most other ambulatory specialties, when we compare them with GPs only on the substitutable drugs they prescribe in common. To optimise the dispensing of generic drugs and thus rationalise healthcare spending, it is necessary to understand these differences and at what level in the drug use the prescriber's specialty comes into play.

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## Availability of data and material

Data used in this study are available as open data (<https://www.assurance-maladie.ameli.fr/etudes-et-donnees/open-medic-base-complete-depenses-medicaments>).

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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